Medical Lib.
SEP 26 1927

VOLUME 34 NUMBER 3

# AMERICAN JOURNAL

OF

# DISEASES OF CHILDREN

EDITORIAL BOARD

CLIFFORD G. GRULEE, Chicago

OSCAR M. SCHLOSS, New York
W. McKIM MARRIOTT, St. Louis
FRITZ B. TALBOT, Boston
L. R. DuBUYS, New Orleans
H. F. HELMHOLZ, Rochester, Minn.

SEPTEMBER, 1927

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $4.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

# CONTENTS OF PREVIOUS NUMBER

## AUGUST, 1927. NUMBER 2


Effect of Therapeutic Doses of Ultraviolet Radiation on Basal Metabolism in Children:
First Paper: Margaret E. Fries, M.D., New York.
Second Paper: Immediate Effect. Margaret E. Fries, M.D., and Anne Topper, M.D., New York.

Enlargement of the Spleen in Children. Adrien Bleyer, M.D., St. Louis.

Pyloric Stenosis of Infants. F. F. Tisdall, M.D. (Tor.); M. W. Poole, M.D., and Alan Brown, M.B. (Tor.), Toronto.

Inorganic Blood Phosphate: Studies of Rats on Rachitic and Nonrachitic Diets. Elizabeth M. Koch, Ph.D., and Meyer H. Cahan, M.S., Chicago.

Papilledema and the Diagnosis of Epidemic Encephalitis. Lester Rosenberg, M.D., New York.

Metabolism of Salts in Nephritis: III. Chlorides and Sodium. Gladys L. Boyd, M.D. (Tor.); Angelia M. Courtney, B.A., and Ida F. MacLachlan, B.A., Toronto.

Hiccups Among Infants. Walter R. Pendleton, S.B., Long Beach, Calif.

Studies in Pubescent Growth, with Special Reference to Periodic Gain. Borden S. Veeder, M.D., and E. H. Rohlfing, M.D., St. Louis.

Renal Infantilism: Report of a Case and a Review of the Literature. F. C. Hunt, M.D., New York.

Chronic Intussusception: An Unusual Type with Prolapse. Oscar B. Markey, M.D., Cleveland, and Katsuji Kato, M.D., Los Angeles.

Progress in Pediatrics:
Diphtheria in Infancy. S. F. Ravenel, M.D., Greensboro, N. C.

Abstracts from Current Literature.

Society Transactions:
American Pediatric Society (Third and Fourth Sessions).

Book Reviews.

Directory of Pediatric Society.


COPYRIGHT, 1927, BY THE AMERICAN MEDICAL ASSOCIATION

American Journal of Diseases of Children

VOLUME 34 SEPTEMBER, 1927 NUMBER 3

# MIKULICZ'S SYNDROME

## A REPORT OF TEN CASES *

ALEXANDER J. SCHAFFER, M.D.

AND

A. WILMOT JACOBSEN, M.D.

BALTIMORE

Almost fifty years ago, Mikulicz [1] reported before the Verein fur Wissenschaftliche Heilkunde a case of chronic, bilateral, painless enlargement of the salivary and lacrimal glands, for the cause of which he could not advance an adequate explanation, but which he believed to be a low grade infection. Report followed report with great rapidity, so that by 1909 Campbell Howard [2] was able to collect reports of eighty-one cases, the clinical characteristics of which corresponded in many ways with those of the one reported by Mikulicz. It had early become evident, however, that although all cases presented the one common feature, i. e., symmetrical enlargement of the lacrimal or salivary glands, they differed widely in many other important particulars. The course in many cases was that of a benign, self-limited condition, whereas in others it was a rapidly fatal one. Pathologically, the material obtained at biopsy or necropsy differed widely in various cases. It became obvious then that the so-called Mikulicz's disease was not a pathologic entity, but a symptom-complex that might follow any number of causes. For the word "disease," the more accurate term "syndrome" was substituted. Von Brunn,[3] in 1905, suggested on an anatomic basis a comprehensive but unwieldy classification, which was later simplified by Campbell Howard. Before discussing this question in detail, we wish to present a series of ten patients seen in the Johns Hopkins Hospital since 1910, six above 14 years of age in the adult services, and four below 14

* Received for publication, March 24, 1927.

* From the Departments of Pediatrics and Medicine of the Johns Hopkins University School of Medicine, and the Harriet Lane Home of the Johns Hopkins Hospital.

1. Mikulicz, J.: Ueber eine eigenartige symmetrische Erkrankung der Thränen-Mundspeicheldrüsen, Beitr. z. Chir., Festschrift, Theodor Billroth, Stuttgart, 1892, p. 610-630.

2. Howard, C. P.: Mikulicz's Disease and Allied Conditions, Internat. Clin. **1**:30, 1909.

3. Von Brunn, M.: Die symmetrische Schwellung der Thränen- und Mund speicheldrüsen in ihren Beziehungen zur Pseudoleukämie, Beitr. z. klin. Chir. **45**: 225, 1905.

years, in the Harriet Lane Home. (Two others, seen before 1910, have been included in Howard's detailed report.)

## REPORT OF CASES

CASE 1.—R. B., a white boy, aged 2½ years, admitted to the Harriet Lane Home, Oct. 10, 1924, because of an eruption over the body, presented the characteristic manifestations of aleukemic lymphatic leukemia. He later developed hypertrophy of the lachrimal, parotid and submaxillary glands and died two months after the onset. Autopsy was performed.

Fig. 1 (case 1).—Beginning enlargement of the parotid and lacrimal glands.

The family history was unimportant. The child was born spontaneously and was healthy at birth; he was fed sensibly, developed normally and had no illnesses until the onset of the fatal one. On Sept. 20, 1924, three weeks before admission, numerous black and blue spots, varying in size from minute petechiae the size of a pin point to areas the size of a half dollar, appeared over the child's body, particularly on the extremities. There were bleeding from the gums and hematuria for a few days. Shortly after this, the glands of the neck and groin gradually increased in size; the patient grew more and more listless and lost his appetite. In the first week of October, the child was seen by his family physician, who diagnosed the condition correctly and performed transfusion three times in rapid succession. His condition was improved appreciably by this treatment; he became more alert, his appetite improved,

and the glands of the neck diminished markedly in size. At the beginning of the illness, daily elevations of temperature were noted.

*Physical Examination.*—On admission, the child presented listlessness, pallor, numerous petechiae of variable age over the skin, moderate general glandular enlargement, several subconjunctival and retinal hemorrhages, and enlarged liver and spleen.

*Examination of the Blood.*—The red blood cells numbered 3,200,000, with moderate anisocytosis and poikilocytosis. The platelets were reduced, numbering 64,000. The white blood cells numbered 800 per cubic millimeter; polymorphonuclears, 6 per cent; large lymphocytes, 45 per cent; small lymphocytes, 49 per cent. No smudges were seen.

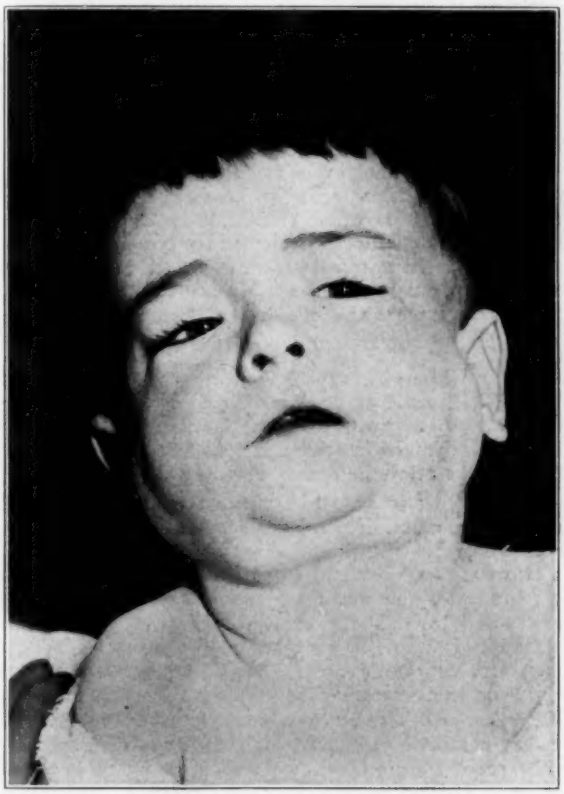


Fig. 2 (case 1).—Appearance of patient shown in figure 1 two weeks later.

Oxidase staining and supravital dye staining corroborated the differential count. Bleeding from a small puncture of the finger continued for fifteen minutes, when it was staunched. Coagulation time was seven minutes by the capillary pipet method.

*Course.*—During the child's stay in the hospital, his general condition grew slowly but progressively worse. His temperature, which for a few days was normal, later became elevated, rising to 103 or 104 F. each evening. The leukocytes increased steadily from 800 per cubic millimeter on admission to 11,000 shortly before death. The differential count remained essentially the same, except that on one occasion the polymorphonuclear leukocytes had risen

to 40 per cent of the total. The lymph glands and spleen rapidly increased in size, the latter extending 8 cm. below the costal margin.

The most interesting development, however, was the progressive enlargement of the salivary glands. On admission, no abnormalities were noted, but on October 17, one week later, obvious fulness could be seen in the parotid region in front of and beneath both ears, and hard, elastic, insensitive tumors could be felt there and below the angles of the jaw in the submaxillary regions. There was no evidence of inflammation, redness and local elevation of temperature or tenderness, and the skin was freely movable over the tumors. These masses became daily more prominent, until by October 20 they gave the face a strikingly bloated appearance. About this time, also, a narrowing of the lid-slits in their lateral halves was noted, and a small tumor the size of a grape could be felt in the site of the lacrimal glands. The sublinguals and the palatal and buccal glands (Blandin-Nuhn) were never visibly enlarged.

Death occurred on Nov. 12, 1924, thirty-two days after admission and fifty-two days after the first symptom was noticed.

*Autopsy Report.*—Grossly, the tremendous enlargement of the parotid, lacrimal and submaxillary glands, as well as the general enlargement of the lymph glands and the extreme pallor were noted. Microscopically, the parenchyma of the lacrimal and salivary glands was found normal except insofar as it was spread apart by the mononuclear cells "which filled all the lymphoid tissue and were scattered practically everywhere else. Smears of the bone marrow showed uniform large mononuclear cells with almost no cytoplasm. The bone marrow of the femur seemed to be a solid mass of lymphoid cells." The suprarenals and the pancreas were the only organs not involved by the infiltrating process.

The diagnosis was acute aleukemic lymphatic leukemia, showing Mikulicz's syndrome.

CASE 2.—G. F., a white girl, aged 2 years, was admitted to the Harriet Lane Home, May 9, 1923, because of "enlarged glands." Besides general glandular enlargement, there was enlargement of the lacrimal and salivary glands. The definite alterations of lymphatic leukemia had taken place in the blood. The child died eight months after the onset. Autopsy was not performed.

*History.*—The family and past histories were unimportant. In December, 1922, six months before admission, the patient had a febrile illness diagnosed as influenza. Following this she appeared nervous, became weak, and lost her appetite. On two occasions she had stomatitis of short duration. She became progressively more pale, and about two months previous to admission, small swellings were noted beneath the rami of the jaw. Somewhat later, other swellings appeared in front of the ears, and at the same time the upper lids were seen to be excessively prominent and the lid-slits narrowed. Several black and blue spots were seen over the body during the week preceding admission.

*Physical Examination.*—The child was fairly well developed but pale, and seemed somewhat apathetic. Symmetrical swellings were present in front of both ears in the parotid region, and were so large as to impart to the face a triangular outline. The skin was pale; there were a number of hemorrhagic spots of variable size and color. The lacrimal glands were readily palpable; the parotid, submaxillary and sublingual glands were greatly and symmetrically enlarged. They were firm, elastic and not tender. The posterior cervical lymph nodes, and the axillaries and inguinals were numerous and shotty. The epitrochlears were not felt. The conjunctivae were not injected; the tonsils were moderately enlarged and were not inflamed. The edge of the spleen was felt just below the costal margin. The liver was not unduly large.

*Examination of the Blood.*—The hemoglobin was 38 per cent; red blood cells, 3,300,000. Some anisocytosis and a diffuse and punctate basophilia were found. One normoblast was seen. The white blood cells numbered 37,400. The differential count showed: polymorphonuclears, 3 per cent; eosinophils, 0 per cent; basophils, 0 per cent; small lymphocytes, 4 per cent; large lymphocytes, 2 per

cent; pathologic lymphocytes, 87 per cent; transitionals, 2 per cent; smudges, 2 per cent. The platelets seemed normal and by count numbered 180,000. The results of the examination of the urine were negative. One-tenth milligram of tuberculin given intradermally gave a negative reaction.

*Course.*—Because of the unfavorable prognosis the child was taken home, where she died several months later.

The diagnosis was acute lymphatic leukemia, showing Mikulicz's syndrome.

CASE 3.—E. P., a white boy, aged 20 months, was admitted to the Harriet Lane Home, Dec. 3, 1924, because of "pallor" and "glandular enlargement" of two months' duration. He presented the signs and hematologic alterations characteristic of acute lymphatic leukemia, as well as enlargement of the lacrimal, parotid and submaxillary glands. He died about five months after the onset of symptoms. Autopsy was not performed.

*History.*—The family history was unimportant, except that the mother's previous pregnancy resulted in a stillbirth. The past history revealed no significant facts. The patient was considered perfectly well until October, 1924, two months before admission. From that time on, he became increasingly pale, lost his appetite and later became apathetic and irritable. Early in November, it was noticed that the glands in the groin were enlarged and tender, and shortly afterward all the other glandular groups were seen to be increased in size. On two occasions, hemorrhagic spots appeared in the skin and twice bright blood was seen in the dejecta. There was a slight rise of temperature in the evening.

*Physical Examination.*—The child was well developed and well nourished but was pale and listless. The face presented a bloated appearance due to protrusion of the upper lids and swellings in the neck at the angles of the jaw and in front of the ears. A few hemorrhagic spots of varying size were seen over the extremities. There was marked glandular enlargement. Besides the involvement of the lymph nodes, the parotid, submaxillary and lacrimal glands were definitely increased in size. The sublingual glands were not palpable. Neither the conjunctivae nor the mucous membranes of the mouth and pharynx were suffused. The spleen was large and firm, extending to the iliac crest on the left and to the midline medially. The edge of the liver was 6 cm. below the costal margin.

*Examination of the Blood.*—The hemoglobin was 24 per cent (Sahli); red blood cells, 1,250,000; the cells were pale and showed marked anisocytosis and poikilocytosis; the white blood cells numbered 30,400. The differential count revealed: polymorphonuclears, 1 per cent; small lymphocytes, 12 per cent; large lymphocytes, 78 per cent; large mononuclears, 3 per cent; smudges, 6 per cent. The platelets were greatly diminished, averaging 35,000. The oxidase stain showed: large granular cells, 7 per cent; large nongranular cells, 82 per cent; small granular cells, 8 per cent; granular smudges, 1 per cent; nongranular smudges, 2 per cent.

As the condition of the patient was regarded as hopeless, the parents removed the child against advice the day after admission. He died soon afterward at home.

The diagnosis was acute lymphatic leukemia, showing Mikulicz's syndrome.

CASE 4.—W. S., a white boy, aged 12 years, was admitted to the Harriet Lane Home, on March 7, 1923, because of "sore, red eyes, fever and enlarged glands." He had had a rise of temperature in the afternoon for three months and sore eyes and painful swelling beneath both ears for one month. Iridochoroditis with enlargement of the parotid glands was found. All the symptoms subsided under combined roentgen-ray and radium treatment. A biopsy was not made.

*History.*—The family history was unimportant, except that the mother had had two miscarriages, one at three months and one at four months, since the

birth of the patient. Except for the usual diseases of childhood, the patient had enjoyed excellent health until the onset of the present trouble. Two years previously, he had had an attack of mumps.

Late in December, 1922, three months before admission, the patient came home from school, feeling bad, with a temperature of 103 F. He remained in bed for a week, with fever, and then returned to school, but a daily afternoon rise of temperature to 100 or 101 persisted. In February, he fainted four times in school and late in that month his eyes became red. Early in March, his mother noticed that the left pupil seemed irregular. About this time, swellings appeared below the ears and increased steadily in size until admission. He complained of pain in those regions, most severe in the evening.

*Physical Examination.*—The boy was well developed and well nourished, in no discomfort and not ill. Both the parotid glands were markedly enlarged, forming visible tumors on both sides. The lacrimal, submaxillary and sublingual glands were not increased in size. Except for chains of glands in both posterior cervical triangles, there was no enlargement of the lymph nodes. The remainder of the examination was entirely negative except for the eyes. The following note was made by Dr. Alan C. Woods: "In the right eye the pupil is dilated and the cornea is entirely clear except for some deposits on posterior corneal membrane in the lower portion of the cornea. The vitreous is clear. The disk is flat and the neuroretinal borders are obscured. There is a good deal of subretinal edema and the retina is decidedly pale near the disk, but no real exudate can be seen. The veins are somewhat over-filled. In the left eye there are deposits on the posterior corneal membrane in the lower half of the cornea. There are some vitreous opacities. The disk is flat but very blurred. Above the disk just below the vein there is a whitish area which appears to be a deep choroidal exudate, but this is the only place where there seems to be any real exudate, although there is a good deal of subretinal edema. The picture is that of a low-grade choroiditis, probably subsiding, with inflammatory deposits on Descemets membrane."

*Examination of the Blood*: The red blood cells numbered 4,352,000; hemoglobin, 82 per cent; white blood cells, 5,400. The differential count (200 cells) showed: Wilson stain; polymorphonuclears, 61.5 per cent; polymorphonuclear eosinophils, 2.5 per cent; polymorphonuclear basophils, 0 per cent; large lymphocytes, 16 per cent; small lymphocytes, 10 per cent; mononuclears, 6 per cent; transitionals, 4 per cent. The cells in smear appeared normal. The platelets were normal in number and appearance.

*Course.*—The patient was referred to Dr. Howard A. Kelly's Sanatorium for radium treatment. He was given four exposures over the parotid glands in rapid succession with the result that they diminished perceptibly in size and the iridocyclitis subsided pari passu. Within two months after discharge from the hospital, i. e., seven months after the onset the enlargement of the parotid glands had completely disappeared. The boy has been seen recently and was found to be in perfect physical condition. The diagnosis was iridocyclitis of unknown origin in combination with Mikulicz's syndrome (febris uveo-parotidea subchronica —Heerfordt).

By way of comparison with these cases, the records of all patients showing Mikulicz's syndrome admitted to the adult service of the Johns Hopkins Hospital were studied. These we present in somewhat less detail.

CASE 5.—E. L., a colored laborer, aged 40, was admitted to the Johns Hopkins Hospital on Jan. 4, 1917, complaining of swelling of the abdomen and shortness of breath. Severe emphysema and arteriosclerosis were found, and the parotid and lacrimal glands were seen to be considerably enlarged. He had acquired syphilis at 18 years of age, and the blood Wassermann reaction was positive. The further course was not known. A biopsy was not made.

*History.*—The patient's history was unimportant, except that his wife had had three miscarriages. He contracted gonorrhea at 14 years of age and had had several subsequent attacks. He had a hard sore on the penis at 18 years of age which lasted six months. There had been some difficulty in breathing since March, 1915, but the definite onset of illness was in December, 1915, when dyspnea became worse and swelling of the legs and abdomen appeared.

*Physical Examination.*—The essential features of the examination were as follows: emphysema, arteriosclerosis and an enlarged heart with occasional extrasystoles. The eyes were prominent, with swollen lids, which drooped so that they were partially shut. The conjunctivae were congested and the lacrimal glands were unusually large. There was fulness in both parotid regions.

*Examination of the Blood.*—The white blood cells numbered 8,600; the differential count showed: polymorphonuclears, 72 per cent; small lymphocytes, 20 per cent; large mononuclears and transitionals, 8 per cent. The blood Wassermann reaction was positive. The patient was discharged improved from the point of view of his cardiac condition, and his subsequent course is unknown.

The diagnosis was syphilis, emphysema, arteriosclerosis and Mikulicz's syndrome.

CASE 6.—P. W., a colored gardner, aged 54, was admitted to the Johns Hopkins Hospital, Nov. 8, 1909, complaining of shortness of breath. There had been mild dyspnea for four years, and for a few days fever and severe dyspnea. An area of pneumonia was found as well as peripheral arteriosclerosis and enlargement of the lacrimal and parotid glands. He had acquired syphilis at the age of 20. Death occurred several days after admission. Autopsy was performed.

*History.*—The family history was unimportant. The patient had a primary sore at 20 years of age, with subsequent alopecia and generalized eruption. There were several attacks of gonorrhea. For about four years before admission, the patient had complained of shortness of breath, with hemoptysis on one occasion. The symptoms increased in severity shortly before admission.

*Physical Examination.*—The patient was obese and dyspneic, with an area of consolidation in the left lung; his heart was enlarged, and there were an aortic diastolic murmur, a collapsing pulse and evidence of myocardial failure. The cervical, axillary and inguinal lymph nodes were enlarged; the epitrochlears were not palpable. The eyelids were puffy, the lacrimal glands producing visible swellings at the outer canthi. The pupils were unequal in size, and reacted sluggishly to light. Both parotid glands were enlarged, firm and slightly tender.

No examination of the blood was recorded. No blood was taken for the Wassermann reaction.

*Course.*—The condition grew rapidly worse, and the patient died two days after admission. At autopsy, chronic endocarditis (aortic valve), aortic insufficiency, subacute adhesive pericarditis, dilatation and hypertrophy of the heart, chronic passive congestion of the viscera, acute lobar pneumonia (left upper lobe), arteriosclerosis, fatty degeneration of the liver, double hydrocele, and hypertrophy of the lacrimal and parotid glands were found.

Microscopic examination of the lacrimal glands showed some increase in connective tissue and several areas of infiltration with small round mononuclear cells. Unfortunately, an especial study was not made of the salivary glands.

The diagnosis was syphilis, arteriosclerosis and Mikulicz's syndrome.

CASE 7.—L. L., a white housewife, aged 43, was admitted to the Johns Hopkins Hospital, April 2, 1924, complaining of "lumps in the neck." Swellings in front of and below the ears and a group of large inguinal glands had appeared and had slowly grown during the two years before admission. The Wassermann reaction was positive, but antisyphilitic treatment failed to reduce the size of the swellings. Radium application brought about their rapid disappearance. Three years after the onset, bloody diarrhea appeared. The patient was readmitted, and abdominal lymphosarcoma was found. Death occurred shortly after admission. Biopsy was made, but autopsy was not performed.

*History.*—The family history was negative except that the patient's husband had pulmonary tuberculosis. She had had one miscarriage (at the fourth month) and, subsequently, four normal pregnancies. Two years before admission, a swelling had appeared beneath the left ear. This steadily increased in size until the time of admission, when a similar swelling was noted on the right side of the neck. Lumps were also seen in the groins.

*Physical Examination.*—The patient was obese, weighing 224 pounds (101.6 Kg.), and had a brassy cough, edema of both legs, mild arteriosclerotic retinal changes, oral sepsis and moderate emphysema. The liver and spleen were barely

Fig. 3 (case 7).—Enlargement of the parotid glands and the cervical lymph nodes.

palpable. The lymph nodes of the anterior and posterior cervical chains were enlarged to the size of cherries. At the angles of the jaw were tumors—in part large lymph nodes, in part parotid glands. The left parotid was the size of a small pear. The right parotid contained nodules the size of hazelnuts, and there were indefinitely outlined masses in the floor of the mouth in the sublingual region on both sides. The inguinal glands were enlarged, and the epitrochlears and axillaries were not palpable. All were elastic and discrete and were neither painful nor tender. The remainder of the examination was negative.

*Examination of the Blood.*—The red blood cells numbered 4,600,000; hemoglobin, 75 per cent; white blood cells, 4,600; the differential count showed: polymorphonuclears, 70 per cent; polymorphonuclear eosinophils, 1 per cent; small

lymphocytes, 11 per cent; large lymphocytes, 6 per cent; large mononuclears and transitionals, 12 per cent. The blood Wassermann reaction was positive.

An excised inguinal gland, examined by Dr. Wylie Forbus, was extensively infiltrated with lymphoid cells with partial obliteration of the germinal centers. The usual cells of the germinal centers were replaced by small lymphocytic cells.

*Course.*—A series of six treatments with arsphenamine failed to affect the size of the glands or the Wassermann reaction. Radium treatment was then instituted, with the result that the glands decreased markedly in size almost to the point of disappearance. Treatment was then abandoned because of coincidental anemia. The differential formula, however, remained unaltered.

Radium treatment was later resumed and was persisted in until the tumors had practically disappeared.

In January, 1925, nearly three years after the onset of the first symptom, an entirely new set of symptoms appeared, namely, diarrhea with blood and mucus in the stools, and a feeling of pressure in the pelvis. The patient was readmitted to the hospital in March, 1925.

On physical examination at this time, there was a swelling at the angle of the left jaw, as large as a hen's egg, a large mass of adenoids and several polypoid masses in the nasopharynx, a large group of glands in the right axilla, and a tremendous tumor within the pelvis. An exploratory operation revealed an inoperable invasive tumor, which on section proved to be a lymphosarcoma.

*Examination of the Blood.*—On Feb. 22, 1925, hemoglobin (Sahli) was 48 per cent; the red blood cells numbered 2,960,000; white blood cells, 5,600; the differential count showed: polymorphonuclears, 67 per cent; polymorphonuclear eosinophils, 1 per cent; small lymphocytes, 12 per cent; large mononuclears and transitionals, 20 per cent.

The patient died on March 21, 1925. The diagnosis was syphilis and lymphosarcoma with Mikulcz's syndrome.

CASE 8.—J. W., a colored laborer, aged 36, was admitted to the Johns Hopkins Hospital, Dec. 22, 1908, complaining of "swollen and painful feet." He had to be readmitted twice because of recrudescence of the same symptoms, which were thought to be due to gonorrheal arthritis. It was noted that his lacrimal, parotid, submaxillary and sublingual glands were all large. He had acquired syphilis at 20 years of age and had a penile scar, although one blood Wssermann reaction was negative. A biopsy was not made.

*History.*—The family history was unimportant. There had been a primary sore at the age of 20, and five gonorrheal infections. Five times during the past twelve years, the patient's feet became swollen. Two weeks before admission, the feet again became swollen and were painful. Following this, both hips and the right thumb became similarly involved.

*Physical Examination.*—At this time, the posterior cervical axillary and inguinal glands were palpable. There was no abnormality of the salivary glands. The involved joints were exquisitely tender and swollen. Scars were noted on the glans penis. The blood examination was normal. The patient was discharged on Feb. 5, 1909, much improved. However, it was necessary to readmit him one month later because the process had not completely subsided.

On this admission the following note was made: The subauricular portions of both parotid glands were distinctly enlarged and firm, both glands being easily grasped between the fingers; the lacrimal glands formed prominences over the outer angle of the upper eyelids; on eversion of the lids nodules the size of peas appeared. The mucous glands on the inner surface of the lips and the sublingual glands seemed much more prominent than normal. Both submaxillary glands were somewhat swollen. A few shotty lymph nodes were present in the neck. The left epitrochlear was palpable; the axillary glands were markedly enlarged.

*Examination of the Blood.*—The red blood cells numbered 4,724,000; hemoglobin, 92 per cent; white blood cells, 12,280.

*Course.*—The patient was discharged again, the condition of the joints being improved. He was admitted for the third time six months later for a recrudescence of the arthritic symptoms. The physical examination was similar to those made previously. The white blood cells numbered 8,800. One blood Wassermann reaction was negative. It was generally agreed that the involvement of the joints was gonorrheal in origin.

The diagnosis was syphilis, gonorrheal arthritis, with Mikulicz's syndrome.

CASE 9.—C. C., a white bank clerk, aged 25, was admitted to the Johns Hopkins Hospital on June 6, 1925, complaining of swelling of the face, which had been

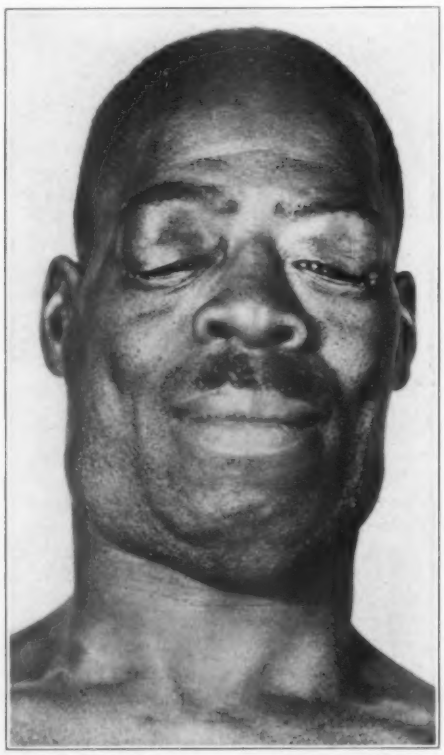


Fig. 4 (case 10).—(Before treatment.) Enlargement of the parotid and lacrimal glands and of the submaxillary and submental lymph nodes.

present for six weeks before admission. Examination was negative except for bilateral painless swelling of the lacrimal and parotid glands. Blood studies showed no abnormalities. The Wassermann reaction was negative. The swellings subsided after two roentgen-ray treatments, and the patient is at present, one year after the onset, perfectly well.

*History.*—The family and past histories were unimportant except for mumps at the age of 9. There was no history of syphilitic infection. About the middle of April, 1925, the patient noticed lumps in front of both ears. The swellings steadily increased in size.

*Physical Examination.*—Nothing abnormal was found physically except the presence of visible enlargements of both parotid and both lacrimal glands, and palpable sublinguals. There was no enlargement of the lymph nodes and the spleen was not palpable.

*Examination of the Blood.*—The red blood cells numbered 4,800,000; hemoglobin was 93 per cent; the white blood cells, 3,600. The differential count showed: polymorphonuclears, 55 per cent; polymorphonuclear eosinophils, 3 per cent; large lymphocytes, 6 per cent; small lymphocytes, 18 per cent; large mononuclears and transitionals, 11 per cent; smudges, 7 per cent. The platelets appeared normal in shape and number. No abnormal cells were seen. The blood Wassermann reaction was negative.

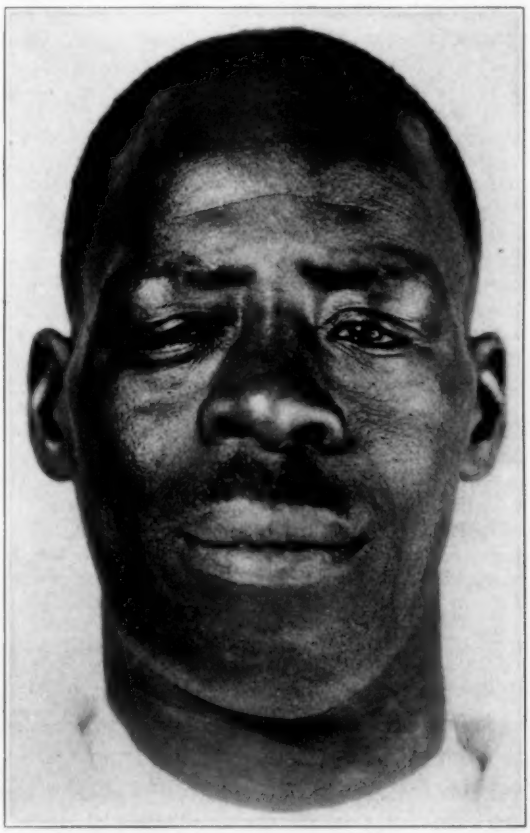


Fig. 5 (case 10).—Same patient as shown in figure 4, after eight radium treatments. The swellings have largely disappeared.

*Course.*—The patient received two roentgen-ray treatments over the parotid glands, and was discharged slightly improved. He was heard from one year after discharge, when he stated that he was perfectly well.

CASE 10.—W. W., a colored laborer, aged 39, was admitted to the Johns Hopkins Hospital on March 29, 1925. Three months before admission, a swelling appeared in the right side of the neck and later in other places. Examination revealed general glandular enlargement and enlargement of the lacrimal and later of the parotid and submaxillary glands. Blood studies revealed alterations characteristic of chronic aleukemic lymphatic leukemia. The swellings subsided under radium but reappeared eight months later. Death followed shortly. Autopsy was not performed.

*History.*—The family history was unimportant. The patient had had a primary syphilitic infection in 1905. Under antisyphilitic treatment, the lesion rapidly healed. Early in January, 1925, three months before admission, a swelling appeared in the right side of the neck, which rapidly increased in size. Other lumps appeared in the neck and elsewhere, and he began to feel weak.

*Physical Examination.*—The patient was well developed and not very ill, and showed a tremendous general glandular enlargement, involving the glands of all the triangles of the neck, particularly the preauricular and postauricular; the axillary, inguinal and femoral glands were also enlarged. The epitrochlear glands at this time were not palpable. The spleen was readily felt. The lacrimal glands were definitely hypertrophied, partially closing the eyes.

*Examination of the Blood.*—On March 30, 1925, the red blood cells numbered 4,720,000; marked anisocytosis and poikilocytosis were present; the hemoglobin was 80 per cent (Sahli); the white blood cells numbered 5,600; the differential count showed: polymorphonuclears, 33 per cent; polymorphonuclear eosinophils, 0 per cent; small lymphoctes, 54 per cent; large lymphocytes, 3 per cent; transitionals and large mononuclears, 6 per cent. No abnormal cells were present.

*Course.*—The patient was exposed to radium on eight occasions, and the lumps rapidly disappeared. Ten months later, however, they recurred with great rapidity.

He was readmitted to the hospital, Oct. 17, 1925. On examination at this time, there were the same glandular enlargements as on the first admission, and in addition enlargement of the epitrochlear, parotid and submaxillary glands.

*Examination of the Blood.*—The white blood cells numbered 10,200; the polymorphonuclears, 19 per cent; polymorphonuclear eosinophils, 2 per cent; polymorphonuclear basophils, 0 per cent; lymphocytes, 70 per cent; large mononuclears and transitionals, 6 per cent; pathologic lymphocytes, 3 per cent.

After two more radium treatments the glands practically disappeared, and the patient was again discharged.

On March 17, 1926, he was readmitted with pneumonia and pneumoccocic septicemia, and died. Radium had been used freely in the interim, so that there were no visible glandular enlargements at this time. No autopsy was obtained.

The diagnosis was chronic lymphocytic leukemia with Mikulicz's syndrome.

## RECAPITULATION

Among these ten patients are four having lymphatic leukemia, three children suffering from the acute form and one adult from the chronic form of the disease. All died within from two to eight months after their first visit.

One patient had lymphosarcoma, and died three years after the appearance of enlargement of the salivary glands.

Another patient suffered from the malady for which Heerfordt [4] coined the term "febris uveo-parotidea subchronica" [5] and recovered com-

4. Heerfordt, C. F.: Ueber eine Febris uveo-parotidea subchronica an der Glandula parotis und der Uvea des Auges lokalisiert und häufig mit Paresen cerebrospinaler Nerven kompliziert, Arch. f. Ophth. **70**:254, 1909.

5. This unusual disease is characterized by symmetrical enlargement of some of the salivary glands in association with an iridocyclitis and often with peripheral nerve paralyses. These symptoms may follow one another in any order; they are usually accompanied by slight fever and mild constitutional symptoms. The disease is self-limited, subsiding generally within from eight to eighteen months, but it may leave the patient with markedly diminished vision. There is a great deal of discussion in the German and Scandinavian periodicals as to its connection with mumps, on the one hand, and tuberculosis on the other.

pletely. This case will be described and the condition discussed in detail in a forthcoming article by Dr. Louis P. Hamburger and one of us.

The four remaining patients must be classed under the heading of Mikulicz's diseases proper, as no definite etiologic agent could be discovered. In one of these, all the possible causative factors were definitely excluded. The three other patients, however, all admitted syphilitic infection; two had scars of the primary infection, and in one the Wassermann reaction of the blood serum was positive at the time of the examination. Syphilis was also present in the other two adults, the patient with lymphosarcoma having a positive Wassermann reaction and the patient with leukemia giving a definite history of the infection. It seems unwise, in the present state of knowledge, to assume that syphilis was the cause of the symptom-complex. Of these four patients, one is entirely recovered, one died of pneumonia shortly after admission to the hospital, and two cannot be traced.

Pathologic material was obtained in only three of the cases—by removal of a lymph node in case 7 and by autopsy in cases 1 and 6.

The lymph node removed in case 7 was "heavily infiltrated with cells of the lymphoid series with partial obliteration of the germinal centers. The usual cells of the germinal centers were replaced by small lymphocytic cells." The pathologist states that exactly the same picture as this may be produced by either lymphosarcoma, leukemia, or simple lymphocytic cells." The pathologist states that exactly the same picture glands in case 1 were the seat of heavy infiltration with lymphocytes, with compression, separation and partial obliteration of the glandular parenchyma. A lacrimal gland in case 6 revealed "some increase in connective tissue and several areas of infiltration with small mononuclear cells."

## PATHOLOGY AND ETIOLOGY

As has been pointed out earlier and as is evident from a glance at the diagnoses of our cases, Mikulicz's syndrome is encountered in a variety of conditions, and its pathologic condition might be expected to vary, as it does, with the etiologic agency.

Quincke,[6] Lafolley,[7] and Léri[8] have described cases occurring in several members of the same family in two succeeding generations. We have no data as to the character of the lesions in these familial cases.

---

6. Quincke: Mikuliczscher Krankheit, München. med. Wchnschr. **53**:47, 1906.

7. Lafolley, P.: De l'hypertrophie simple des glandes parotides. Paris, 1894, p. 45.

8. Léri, A., and Gutmann: Hypertrophie simple, congénitale, familiale, héréditaire et régionale des diverses glandes salivaires ("mangy" algérien?), Bull. et mém. Soc. méd. d. hôp. de Paris **34**:368, 1912.

Tuberculosis has long been suspected of playing an important part in the causation of the syndrome, and undoubtedly in certain cases it is difficult to gainsay the evidence presented. Krailsheimer [9] demonstrated tubercles and tubercle bacilli in the enlarged parotid glands of his patient, as did Plitt [10] somewhat later. Napp,[11] and recently Gjessing,[12] have demonstrated typical tuberculous lesions in tissues from the eyes of their patients, in both of whom ocular manifestations accompanied hypertrophy of the salivary glands. These form, however, only a minority of the total number of cases, and by no means prove the point that tuberculosis is the sole etiologic agent of the syndrome, as some of the German observers would have us believe.

Syphilis has claimed its share of the attention and Osler,[13] Lintz,[14] Gutmann,[15] Posey,[16] Bourges,[17] and a great number of others have described patients in whom evidences of this disease accompanied the syndrome in question. Lintz's patient had a strongly positive Wassermann reaction—and a negative tuberculin reaction—and at autopsy the parotid glands contained "necrotic areas with giant cells and round cell infiltration destroying the gland structure." Whether this was gummatous in nature we cannot say. This patient was not improved by arsenic treatment, but Gutmann's patient responded rapidly to potassium iodide. Unfortunately, the diagnosis of syphilis pathologically is not so easy as that of tuberculosis, and we may have to wait until some positive evidence, such as the demonstration of the treponema in the glands, is brought forth before its etiologic rôle can be definitely established. The evidence is by no means conclusive then, that syphilis, per se, can give rise to the syndrome, but the incidence of syphilis is so high in the cases reported as well as in our series that the association seems more than purely accidental.

---

9. Krailsheimer, A.: A Case of Mikulicz's Disease, with Pronounced Tubercle of the Iris, Ophthalmoscope **6**:172, 1908.

10. Plitt, W.: Ueber Tuberkulose der Tränendrüsen, Klin. Monatsbl. f. Augenh. **43**:40, 1905.

11. Napp, O.: Ueber die Beziehungen der Mikuliczschen Erkrankung zur Tuberkulose, Ztschr. f. Augenh. **17**:513, 1907.

12. Gjessing, H.: Ueber Tuberculose als Aetiologie bei der sog. Febris uveoparotidea (Heerfordt), Klin. Monatsbl. f. Augenh. **60**:249, 1918.

13. Osler, William: On Chronic Symmetrical Enlargement of the Salivary and Lachrymal Glands, Am. J. M. Sc. **115**:27, 1898.

14. Lintz, W.: Von Mikulicz's Disease, New York State J. M. **11**:67, 1911; Von Mikulicz's Disease; Further Studies, J. A. M. A. **61**:1621 (Nov. 1) 1913.

15. Gutmann, A.: Mikulicz'sche Krankheit in ihrer Beziehung zur Lues, Berl. klin. Wchnschr. **44**:1141, 1907.

16. Posey, W. C.: Notes on a Case of Symmetrical Lymphomata of the Lacrimal and Salivary Glands (Mikulicz's Disease), Ophth. Rec. **25**:286, 1916; Mikulicz's Disease. [Symmetrical lymphoma of the lacrimal glands]. Tr. Coll. Phys., Philadelphia **38**:345, 1916.

17. Bourges, H.: A propos de deux cas de syndrome de Mikulicz et de leur interprétation pathogénique, Bull. et mém. Soc méd. de hôp. de Paris **48**:854, 1924.

In leukemia, the salivary and lacrimal glands seem to be affected in exactly the same manner as the liver, kidney and some other organs commonly are affected; namely, by infiltration and replacement of the parenchyma with lymphocytic cells. It is a remarkable fact, and its explanation is not at all clear, that no reports are to be found in the literature of cases of the syndrome associated with leukemias of the myeloid type.

Fig. 6 (case 1).—Section of a submaxillary gland, showing infiltration of the parenchyma with lymphocytic cells.

The pathologic changes in the glands found in cases of chronic plumbism and iodism, diseases which without question can cause the development of the syndrome, we have not found described.

In those cases for which no etiologic factor can with any degree of assurance be found, the so-called Mikulicz's disease proper, the pathologic picture resembles one or the other of two types. Either one finds an

increase in the lymphoid elements in the glands—either diffusely, or in small aggregations, or both—or, rarely, a hyperplasia of the connective tissue elements, with ultimate diffuse scarring. The latter is by many considered the end-stage of the former. The finding of these two types of reaction has given rise to the difference of opinion as to the etiology of Mikulicz's disease proper, some holding with Milkulicz that it is a

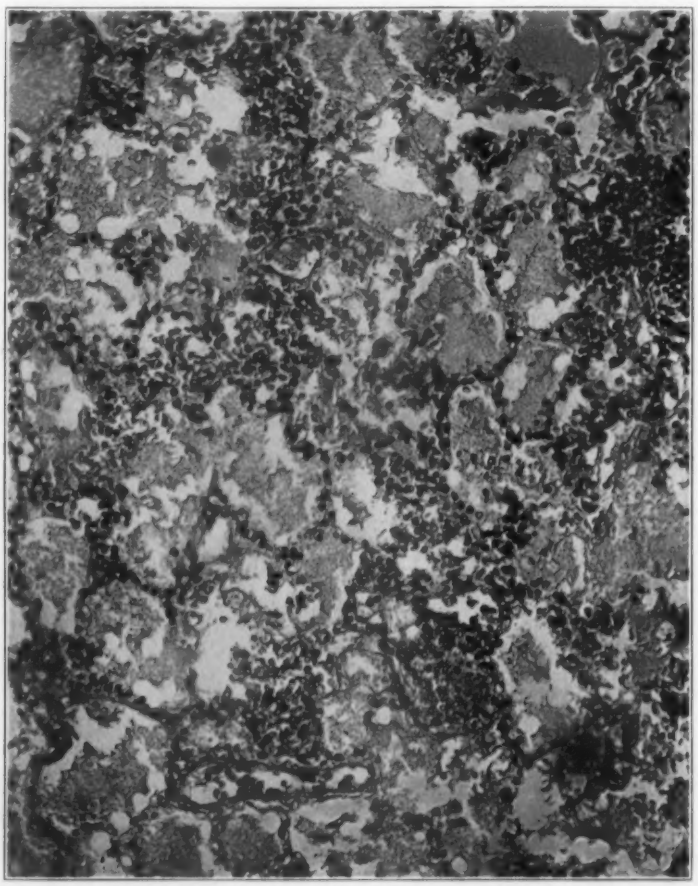


Fig. 7 (case 1).—Section of lung. The walls of the alveoli show lymphocytic infiltration similar to that seen in the salivary glands.

chronic inflammation; others that it is a benign new-growth. The former view is the most popular and is given strong support by the frequent occurrence of inflammatory lesions in the conjunctivae and mucous membranes of the upper respiratory tract as immediate precursors of the glandular swellings and by the long-continued, often febrile, course, with its usual termination after some months or years in spontaneous cure.

The argument in favor of syphilis or tuberculosis as the offending agents in this type of the disease must be considerably strengthened before much consideration can be afforded them.

COMMENT

In 1904, Campbell Howard [2] attempted a simple classification of all the cases presenting Mikulicz's syndrome that he could find in the literature, and on its basis he elaborated a theory that has dominated the literature on the subject since that time. He divided all the cases into three groups, with the captions Mikulicz's disease proper, pseudoleukemia, and leukemia.

In his first group, he included all those patients who presented swelling of the lacrimal or salivary glands, but no lymphadenopathy, no enlargement of the spleen, and no significant alterations in the blood. The definition is so broad, however, that homogeneity is lost, for within the group must be placed cases on an heredofamilial basis, as well as others in which the etiologic relationship of syphilis and tuberculosis, and even gout, plumbism and iodism, can scarcely be doubted. To these, the name Mikulicz's disease should assuredly not be applied. This name should be given only to those instances of the syndrome in which the most painstaking search has failed to discover any of the known possible exciting factors. In the group that is left will be found patients whose clinical characteristics bear a striking resemblance to one another. These are most commonly adults (87.3 per cent in Howard's series). They frequently suffer first from some "eye trouble;" a low fever is common, especially at the onset; pain and tenderness of the glands are rare. The swelling of the glands tends to subside after a period of from four months to two years, and may be successfully treated by roentgen-ray exposure or excision.

To Howard's second group, termed pseudoleukemia, were relegated those cases in which, besides the salivary enlargement, local or general enlargement of the lymph glands or enlargement of the spleen, or both, were present. The choice of the term "pseudoleukemia" is in itself unfortunate, as it was used originally by Cohnheim to designate a condition of marked lymphadenoid hyperplasia, in the glands and adenoid tissue throughout the body, without blood changes, and shortly after began to be used as a synonym for Hodgkin's disease. The line of demarcation between groups 1 and 2 is of necessity vague, as the degree of glandular enlargement sufficient to rule a case out of the first group and make of it a pseudoleukemia is difficult to define. Again, some cases are beyond question classed with the latter group because of lymphadenopathy or splenomegaly due to purely coincidental conditions, such as syphilis and malaria. Finally, one finds a certain number classed in this group which are now known to represent unrecognized instances of

aleukemic leukemia. The great majority of these patients have the same histories, present practically the same physical characteristics and run courses similar to those comprising the first group, the only difference frequently being a slight hyperplasia of the lymph glands or a somewhat enlarged spleen, both of which may be purely accidental.

Howard's third group is formed by those patients who have definite leukemia. These are of especial interest to us for two reasons, because in the literature examples are so infrequently encountered, and because the great majority of these patients are children. Beyond a doubt, a great many cases that have been classified as pseudoleukemia should have been placed in this division with the aid of more complete blood studies or by placing a more correct interpretation on the results of the examination of the blood. Von Brunn's [3] case, mentioned in the foregoing, is one example of this error, as are those of Battle,[18] Stock,[19] Moorehead,[20] and Paton.[21] Paton explained the changes in the blood of his patient (which showed 20,00 white blood cells with 85 per cent lymphocytes and numerous smudges) by assuming that the tremendously enlarged salivary glands were converted into factories for lymphocytes, which poured these cells into the circulation. That just the reverse is true, namely, that the glands are themselves enlarged because they enmesh innumerable lymphocytes from the circulating blood, is apparent from a consideration of case 1. Here, although the salivary glands became progressively larger, the leukocyte count fell steadily, reaching at one time the astonishing level of 800 per cubic millimeter. There is nothing whatever to differentiate these cases of leukemia from others in which involvement of the salivary glands is absent. It merely happens that in these cases the heavy infiltration with lymphocytes, which is commonly present in the lymph glands and in some of the other tissues in leukemia, involves also the salivary and lacrimal glands.

In his conclusion, Howard elaborates the theory of the progression of Mikulicz's disease from the disease proper, through a pseudoleukemic stage, to leukemia, a possibility earlier suggested by Wallenfang [22] and Von Brunn.[3] He says, in part: "A whole series of cases exists forming links in the chain from isolated lymphomata . . . to complete involvement of these glands with simultaneous disease of the lymphatic and hematopoietic system." He goes on to say that "Mikulicz's disease

---

18. Battle, W. H.: A Case of Mikulicz's Disease, Proc. Roy. Soc. Med. London (Clin. Sect.) **5**:171, 1911-1912.

19. Stock, W.: Ueber Augenveränderungen bei Leukämie und Pseudoleukämie, Klin. Monatsbl. f. Augenh. **44**:328, 1906.

20. Moorehead, T. G.: An Unusual Case of Mikulicz Disease, Dublin J. M. Sc,. **2**:595, 1921-1922.

21. Paton, L.: Case of Mikulicz's Disease, Proc. Roy. Soc. Med. London (Ophth. Sect.) **8**:28, 1914-1915.

22. Wallenfang: Beitrag zur Lehre von der symmetrischen Erkrankung der Tranen- und Mundspeicheldrüse, Virchows Arch. f. path. Anat. **176**:90, 1904.

is a clinical entity which may run its course with or without involvement of the lymphatic and hematopoietic systems." This concept, though suggestive from the anatomic point of view, seems entirely unwarranted by the evidence at hand. Two cases, those of Stock [19] and Marcuse,[23] are cited as proofs of the progression. Stock's patient, "Lorenz," was an elderly man who, on first examination, showed enlargement of the parotid and lacrimal glands, periosteal tumors, and a cutaneous eruption; at that time, his blood showed a "moderate anemia, no leukocytosis, but a relative and absolute increase in lymphocytes," whereas six months later there were 53,000 white blood corpuscles with 76 per cent lymphocytes. "Hence," says Howard, "the case was first pseudoleukemia with later development into chronic lymphatic leukemia." Obviously the patient had first and last a chronic lymphatic leukemia, but at the time of the earlier examination he was in an aleukemic stage. Marcuse's case is somewhat different. His patient, a boy, aged 11 years, had at the first examination enlargement of the lacrimal and all the salivary glands. His white blood cell count was 6,000 with 63 per cent polymorphonuclears and 24 per cent lymphocytes, an essentially normal distribution. One and a half years later the child died after a rapidly developing myocardial insufficiency with anasarca. At autopsy, tremendous enlargement of the mediastinal glands as well as of the salivary glands was found, the increase in size being due to "reine hyperplasie," pure overgrowth of the lymphocytic elements. It is difficult at this time to diagnose, but the case seems remarkably similar to L. L., in case 7 of our series, who first noticed glandular enlargements in 1922 and died three years later of what proved to be definite abdominal lymphosarcoma.

That the leukemia, when it does occur, is invariably primary, seems to us the much more likely explanation, and that pathognomonic hematologic alterations will be invariably found by the time Mikulicz's syndrome has developed we feel no doubt. The course of events in case 1 was simple enough. The child came to us with well developed manifestations of leukemia; several weeks later, the parotid and lacrimal glands became enlarged, and at autopsy exactly the same type of infiltration was found in these glands as that in the liver, kidneys and lung. Our feeling, then, is that though every case of Mikulicz's syndrome is possibly one of leukemia, Mikulicz's disease proper is not potential leukemia.

## CLASSIFICATION

Howard's classification, then, though simple, is misleading, largely because of its simplicity. Von Brunn's is a purely anatomic one, and is

23. Marcuse, P.: Ein Fall von Mikulicz'scher Krankheit (symmetrische Anschwellung der Thränen- und Mundspeicheldrüse), Berl. klin. Wchnschr. **41:** 1205, 1904.

extremely unwieldly. In 1915, Thursfield [24] made the first attempt to classify the syndrome on an etiologic basis. He divided all the cases showing enlargement of the salivary glands into eight groups, as follows: (1) a congenital, familial and hereditary condition; (2) Mikulicz's disease proper; (3) Mikulicz's disease with involvement in the lymphatic apparatus; (4) leukemia; (5) tuberculosis; (6) syphilis; (7) gout, and (8) sialodochitis fibrinosa. This classification includes practically all the conditions in which Mikulicz's syndrome occurs, but by placing all the groups on the same plane, fails to emphasize properly the important conditions or to relegate the unimportant ones to a minor position. It seemed to us wiser, therefore, to classify the syndrome in much the same fashion as has been done for the purpuras, by dividing them into two large groups, a symptomatic and an idiopathic, as follows:

I. Mikulicz's Disease
   *A.* Familial
   *B.* Mikulicz's Disease proper
II. Mikulicz's Syndrome
   *A.* Leukemia
   *B.* Tuberculosis
   *C.* Syphilis (?)
   *D.* Lymphosarcoma
   *E.* Toxic
      1. Lead
      2. Iodides, etc.
   *F.* Gout (?)
   *G.* Febris uveo-parotidea subchronica

SUMMARY

1. Ten cases of Mikulicz's syndrome have been presented in some detail. Their pathology and etiology have been discussed.

2. A classification has been suggested in which the cases are divided into two groups: (1) symptomatic and (2) Mikulicz's disease proper. It has been proved that leukemia, lymphosarcoma, and tuberculosis can produce this symptom-complex, whereas the proof that syphilis can produce it is less convincing.

3. The exact nature of Mikulicz's disease proper is still in doubt. It seems likely that it is a low-grade infection, running a slow course, with spontaneous termination, but its etiology remains to be demonstrated.

4. Evidence has been presented against the time honored theory of the progression of Mikulicz's disease from the disease proper, through pseudoleukemia to leukemia.

---

24. Thursfield, H.: Bilateral Salivary Swellings (Mikulicz's disease): A Clinical Review, Quart. J. Med. **7**:237, 1913-1914.

# ANEMIA IN CHILDREN

## WITH SPLENOMEGALY AND PECULIAR CHANGES IN THE BONES
## REPORT OF CASES *

THOMAS B. COOLEY, M.D.

E. R. WITWER, M.D.
AND
PEARL LEE, M.D.
DETROIT

Five of the seven cases to be described were presented at the meeting of the American Pediatric Society, in 1925;[1] the other two have come to our attention more recently. They have enough common and distinctive features to lead us to believe that they can be classed properly in the same group, and the patients present certain peculiar appearances, not especially noted heretofore in the literature of the anemias, which seem to us well worth recording.

The thing that first led us to distinguish these children was their peculiar appearance. They resembled the mongolian race distinctly. This characteristic, on analysis, proved to be due partly to a muddy, yellowish discoloration of the skin and partly to a thickening of the cranial bones and the malar eminences; the thickening was more pronounced when the progress of the disease had been more rapid in the earliest years. This peculiar appearance has led in two cases to a tentative diagnosis being made in the polyclinic, which proved correct on further study. The thickened bones give a characteristic appearance in the roentgenograms, readily recognized by the roentgenologist. The long bones also present striking changes. Observation of the peculiarities of the bones led to some studies of blood chemistry and metabolism, which have given us no definite information.

In all of the children, the condition was similar to that description of von Jaksch's anemia which seems to be generally recognized by those who consider this disease a definite clinical entity. That is to say, the cases began in infancy with moderate anemia, pronounced splenomegaly, leukocytosis of varying degree, many normoblasts, and normal or decreased fragility to salt solutions. Reticulated cells were not always studied, but when looked for were found markedly increased. In all, the disease was essentially chronic, and in most of the cases there was no apparent reason for grave secondary anemia.

---

* Received for publication, Nov. 2, 1926.

* From the Children's Hospital of Michigan.

1. Cooley, T. B., and Lee, Pearl: A Series of Cases of Anemia with Splenomegaly and Peculiar Bone Changes, Tr. Am. Pediat. Soc., 1925.

Patients 1 and 2 were sister and brother, born of Italian parents who spoke practically no English. The father, mother and two older children were living and well. One child died at the age of 5 of an unknown cause. The Wassermann reaction of the father was 4 plus. The Wassermann reaction of the mother and of the other children was negative. The family history otherwise was unimportant.

## REPORT OF CASES

CASE 1.—*History.*—B. R., aged 3½ years, was brought to the polyclinic, June 30, 1921, and was admitted at once to the hospital. The chief complaint was progressive enlargement of the bones of the head and face, first noted at about the age of 10 months. Pallor and enlargement of the abdomen had also been noted by her parents. Her color was said to have changed with the first dentition.

No other history was obtained, except that she had been born at full term, of normal labor, and had been nursed, with adequate additional feeding, for twenty months.

*Examination.*—The child was small and somewhat undernourished, weighing 24¼ pounds (11.2 Kg.). The head was strikingly large, measuring 45 cm. in circumference. The enlargement was most marked in the cranial and malar bones, which were prominent. The skin was a muddy yellow, and there was a yellow tinge to the sclerae. These peculiarities gave the child a distinctly Chinese appearance.

The abdomen was large, distended and tense. The spleen was large, extending a hand's breath below the ribs and nearly to the midline; it was smooth, firm and not tender. The liver was only slightly enlarged on admission, but grew rapidly while the child was under observation. It was moderately firm and smooth. Little else of importance was noted. The tonsils had been removed. There were a few slightly enlarged lymph nodes. The extremities were thin, and the musculature was poor. The heart and lungs were normal. There were no indications of antecedent rickets. Repeated Wassermann tests were negative, as was also the Pirquet test.

The child remained in the hospital from June 30 to August 12; she was readmitted September 6 and died October 10.

During the first period she was considered probably syphilitic, owing to the positive Wassermann reaction of the father, and was given intensive treatment without result. She developed a pericardial effusion at one time, and at another had a mild fever without definite cause.

Her blood, as well as that of her brother, did not receive the detailed study that was given that of the patients seen later, especially with regard to evidence of hemolysis. The counts were fairly constant. The hemoglobin varied from 30 to 40, and the red cells from 2,250,000 to 3,200,000. The color index was always low. Poikilocytosis and anisocytosis were present. Polychromatophilia was not noted, and the patient was the only one in the series who never showed nucleated red cells. We attributed these facts to the erythropoietic portion of the marrow having reached a stage of extreme exhaustion before the child came under observation. The white cells numbered from 30,000 to 54,000, with usually a slight predominance, as high as 60 per cent, of small lymphocytes. Myelocytes were seen once.

On readmission, the patient was considered as possibly having an atypical leukemia. The anemia became more marked, with the hemoglobin content 20 per cent a few days before death. The leukocytes never were more than 54,000, and the maximum lymphocytosis (60 per cent) was observed soon after the child was first admitted to the hospital, while toward the end the white cells diminished in number. The heart became enlarged, with a systolic murmur, and there was a general terminal edema.

Throughout the stay in the hospital the urine was negative for bile and urobilinogen. It was usually alkaline, and often dark brown. Unfortunately, it was not examined for hemoglobin or hematin. The stools were dark.

Only ordinary treatment was given, with the exception of mercury and arsphenamine.

The reports of the examination of the tissues are given later, with those of the patient's brother. The roentgenographic observations in all of the patients will be considered together.

Fig. 1 (cases 1 and 2).—Appearance of sister and brother, at 3½ years and 11 months, respectively.

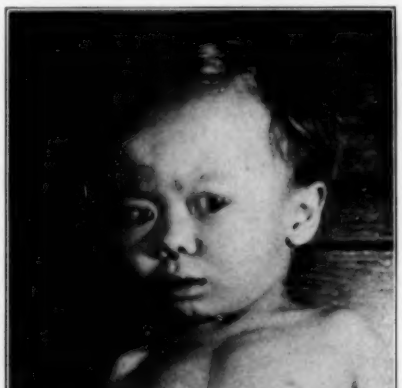


Fig. 2 (case 2).—Appearance at 2 years and 9 months.

CASE 2.—*History.*—M. R., aged 11 months, was first seen, June 30, 1921, with his sister (case 1). He had apparently been normal at birth, had been nursed for ten months, and then had been put on a full diet. At 8 months the mother noticed a change in his color and took him to a clinic, where she was told that he had a large spleen. He was admitted to the Children's Hospital with his sister with the diagnosis of probable syphilis.

*Examination.*—The boy was well nourished and weighed 18 pounds (8.2 Kg.). The head was not noticeably large, but the skin had an icteric tinge not noticed in the sclerae. He appeared anemic. There were five teeth; the fontanel was normal,

and there were neither gross nor roentgen-ray evidences of rickets. The lungs were normal. The heart showed a soft systolic murmur. The abdomen was distended. The spleen was felt three fingerbreaths below the ribs and was smooth and not tender. The liver was palpable 2½ inches below the ribs.

The hemoglobin content of the blood was 48; red cells, 2,520,000; white cells, 12,500; polymorphonuclears, 60; small lymphocytes, 32; lymphocytes, 8. The coagulation time was two minutes.

Several Wassermann tests were negative, but antisyphilitic treatment was given until August 12, when the boy was discharged, unimproved, to the polyclinic, where he was observed until March 24, 1923, readmission to the hospital frequently being advised and refused. During this period there was one doubtful Wassermann reaction, 4 plus to cholesterinized antigen and negative to the Noguchi test. Other reactions were wholly negative. There was no change in the blood picture. The head was observed to grow larger. The liver and spleen increased somewhat in size. The patient had frequent respiratory infections. Various blood counts showed: red blood cells, 2,000,000; white blood cells, from 16,000 to 32,000; polymorphonuclears, from 50 to 55; small lymphocytes, from 40 to 46; large lymphocytes, from 3 to 5; hemoglobin content, from 35 to 40.

The boy was readmitted, March 24, 1923, at the age of 2½ years. The head was large (it was not measured) and was distinctly of the same type as that of the sister (case 1). The long bones also showed the same peculiarities. The heart and lungs were unchanged. There were a few lymph nodes the size of a pea.

Examination of the blood revealed: hemoglobin, 30; red blood cells, 2,800,000; white blood cells, 41,600; many nucleated red cells; polymorphonuclears, 42; small lymphocytes, 53; large lymphocytes, 5; blood calcium, 5; the blood phosphorus was too little to estimate. Fragility showed: hemolysis began in 0.3 per cent and was not complete in 0.2 per cent.

*Course.*—The boy was given a transfusion on March 28, without perceptible improvement. On April 4, the spleen was exposed to deep roentgen-ray therapy. Immediately following this the patient developed fever, due to cervical adenitis; the glands suppurated and were opened and the condition became steadily worse. On May 2 he was given another transfusion, which also did not cause improvement. The heart became dilated, edema developed and the child died on May 15. Throughout the last stay in the hospital, nucleated red cells were a predominant feature in the blood picture. The urine, like that of the sister, often was noted to have an unexplained dark color, which, after observations in cases 3 and 4, we believe probably to have been due to hematin.

Case 3.—(From Dr. Abt's clinic at the Michael Reese Hospital; reported by Dr. O. T. Schultz.) *History.*—F. C. (from his name probably a Syrian), aged 2½ years, was admitted to the Michael Reese Hospital, Oct. 24, 1921. The clinical diagnosis was chloroma, and the anatomic diagnosis was pseudoleukemia infantum (von Jaksch's anemia).

*Clinical History.*—The patient had been bottle fed since birth, which was normal. He had been restless and fretful since 4 months of age. At about 8 months of age, the parents thought that the child's abdomen became more prominent than normal, a condition that had persisted. On admission, the skin felt doughy. The head appeared large, especially in its transverse diameter; the fontanels were closed. The abdomen was tender; the liver extended two fingerbreadths below the costal margin. The cervical glands were moderately enlarged.

*Examination of the Blood.*—The blood count revealed: red cells, 2,020,000; hemoglobin content, 35 per cent; leukocytes, 18,000. In a differential count of 200 cells, there were 46 per cent neutrophil polymorphonuclears, 38 per cent small lymphocytes, 3 per cent large mononuclears, 1 per cent transitionals, 2 per cent eosinophils, 1 per cent basophils, 9 per cent myeloblasts and a number of degenerated large cells with vacuolated cytoplasm, considered either myeloblasts or

endothelial cells. There were 5 normoblasts; poikilocytosis and anisocytosis were present. On succeeding days the red cell count gradually decreased to a minimum of 1,360,000 on November 16. Myelocyte and myeloblast counts of as high as 67 per cent were made; when these cell counts were high, the polymorphonuclear counts were low. The condition of the red cells remained similar to that noted in the first examination, with from 1 to 4 nucleated red cells found in a count of 100 cells (white); toward the termination of the case nucleated red cells disappeared, as did most of the myelocytes, the polymorphonuclear neutrophil percentage running from 45 to 60 per cent. The total leukocyte count varied somewhat; most often the figures were between 20,000 and 30,000, sometimes from 12,000 to 15,000, and once 31,000. On the day before death the red cell count was 1,100,000; hemoglobin content, 25 per cent; leukocytes, 10,200, with 55 per cent neutrophil polymorphonuclears and 2 per cent myelocytes. The blood picture suggests an anemia with little erythropoiesis, but with some leukocytopoiesis in the earlier stages, with later exhaustion of the functions of the tissue which form both the red and white cells. Throughout most of the course of the disease, the temperature varied from 99 to 100, with occasional sudden increases to 106 F., on October 29, and to 103, on November 8, 12 and 17, and December 8. The Wassermann reaction of the blood was negative.

*Postmortem Examination.*—We summarize here the important features of Dr. Schultz's report. His description and the sections that he sent us correspond so exactly to Dr. Witwer's observations in our cases 1 and 2 that they are sufficient for all three case reports, with the exception that the fibrosis of the spleens of our patients was so extensive that Dr. A. S. Warthin, to whom we submitted them, was inclined to think them syphilitic; however, he saw no evidence of syphilis in other organs, and did not believe that the rest of the symptoms could be explained by the presence of syphilis.

"In sawing through the calvarium, one was impressed by the unusual thickness of the skull; in spite of the increased thickness the bone was easily sawed. The convex surface of the parietal bones had a stippled appearance, like that of pigskin, due to the fact that the redder cancellated bone was seen through the thin outer layer of compact bone. The dura, which was not abnormally adherent, had an increased amount of clear fluid present beneath it. The pia was thick and edematous. As the brain was brought to view within the cranial cavity it appeared small, but this appearance was only relative and was due to the marked thickening of the bones. The fontanels were closed and the sutures could not be seen. The calvarium was from 1 to 1.7 cm. thick; it was thinnest in the left occipital region and thickest in the frontal region. On cross-section, the bone, of a pinkish color, appeared to be largely spongy; its spaces, however, were small and close. The inner surface was covered by a layer of pale compact bone, less than 0.5 mm. thick. The outer surface was covered by an even thinner layer of compact bone. The supra-orbital plates of the temporal bones were from 4 to 7 mm. thick and had the same structure as the bones of the calvarium.

*Microscopic Examination.*—The malpighian bodies of the spleen were small. Each had a relatively large, palely stained center which was composed of large oval and elongated spindle cells. Nuclear fragments were intermingled with these cells; the appearance of the center suggested exhaustion of the lymphoid follicles. The tissue between the malpighian bodies was strikingly and uniformly dense, and appeared diffusely fibrous; this tissue was composed chiefly of oval and spindle connective tissue cells and contained few lymphoid cells. In the dense pulp were numerous cleft-like sinusoids lined by prominent cuboidal endothelium. In scattered, ill-defined areas, the elongated cells of the pulp contained finely granular, dark brown pigment. Moderate numbers of eosinophils were scattered about in the dense pulp. Anything suggestive of myeloid or lymphoid transformation of the spleen was entirely absent. Microscopically the spleen was an exact duplicate of the colored illustration that Eppinger gives as characteristic of the spleen in pseudoleukemia infantum.

The liver cells were moderately swollen. Their cytoplasm did not stain deeply and had a foamy, vacuolated appearance. Many of the cells, especially at the centers of the lobules, contained finely granular, light brown pigment. The Kupfer cells and the endothelium of the sinusoids contained more coarsely granular and darker pigment. The tissue was free from cellular reaction.

In the ribs, the costocartilaginous junction and the zone of the preliminary calcification were normal. The layer of the cortical bone was thin. The spongy, major portion of the bone was composed of broad, prominent, anastomosing trabeculae of normally formed bone. The spaces between the trabeculae were filled with cellular marrow. In the latter, polymorphonuclear leukocytes predominated. A fair proportion of the cells were large, with large vesicular nuclei and clear, faintly stained cytoplasm. Transitional stages between such cells, which apparently were myeloblasts, and the typical polymorphonuclear leukocytes were seen. Such cells had round or indented nuclei and a smaller rim of cytoplasm which was granular; these apparently were myelocytes. Multinucleated giant cells with deeply stained nuclei were fairly numerous. These were scattered about among the other cells and were not applied to the bone; they were megakaryocytes rather than osteoclasts. There were few cells which could be identified definitely as red cell precursors. At the margin of the bone, just beneath the cortical layer, some of this tissue had replaced most of the homopoietic tissue present elsewhere in the marrow spaces. The bones of the skull had the same general structure as the ribs. The outer layer of cortical bone was thicker and formed a complete layer. Between the two cortical layers the bone was composed of an anastomosing network of broad bone trabeculae. The spaces between the trabeculae were filled with cellular marrow identical with that in the ribs. Replacement of cellular marrow by young connective tissue, of the character of osteoid tissue, was more marked in the bones of the skull than in those of the ribs. In the thickened supra-orbital plates, the same process was present as in the rest of the bone.

*Comment.*—The microscopic structure of the spleen, the blood picture during life and the structure of the bone marrow appear to relate this case more closely to a von Jaksch pseudoleukemia infantum than to any other known condition. The change that occurred in the bone marrow is interpreted as an aplasia of erythroblastic marrow and a hyperplasia of leukoblastic marrow. The partial replacement of cellular marrow by cellular connective tissue of the osteoid type indicates beginning exhaustion of the hyperplastic process present. From the gross examination, no plausible relation of the changes in the bones of the skull to the rest of the pathologic picture could be thought of. The microscopic examination, however, apparently makes the changes in the bones of the skull a definite part of the general process. The flat bones of the skull participated in the same hyperplasia of leukoblastic marrow as characterized the long bones; there was the same absence of erythroblastic hyperplasia, and the same increase in the amount of spongy, trabeculated bone. It is believed, therefore, that the changes in the bones of the skull were part of the same process that was involving the hemopoietic system as a whole."

CASE 4.—*History.*—R. A., an English girl, aged 3 years, was brought to the polyclinic because of an earache on April 26, 1922, and was admitted to the hospital with the diagnosis of "pseudoleukemic anemia."

Her father contracted syphilis before his marriage, eleven years before the child's birth, and at the time of the child's admission to the hospital was an inmate of a county institution because of some cerebral condition. The child's mother, who was not especially intelligent, seemed in perfect health. She had had three healthy children before this one, and several self-induced abortions but no miscarriages. She had had numerous Wassermann tests, all of which were negative. The family history otherwise was unimportant.

The patient had been breast fed, with additional feedings, for fifteen months. She had her first tooth at 5 months and walked at 2 years. She was said always to have been sickly; she did not grow as the other children did and was backward

in play. Her color had been "queer" from early infancy. She had had measles, varicella and bronchitis, and was subject to colds and sore throats.

*Examination.*—On admission, the child was undersized and stupid, and weighed 28 pounds (12.7 Kg.). The skin was a muddy, brownish yellow. The sclerae were faintly tinged. The peculiarities in the shape of the head and the facial appearance were not noted at that time. The tonsils were diseased. The spleen was large, smooth and firm, reaching nearly to the umbilicus. The liver was enlarged only slightly. Nothing else of especial interest was noted, and there were no indications of old rickets.

*Examination of the Blood.*—This revealed: hemoglobin content, 36 per cent; red blood cells, 2,900,000; white blood cells, 26,000 polymorphonuclears, 65 per cent; small lymphocytes, 28 per cent; large lymphocytes, 6 per cent; eosinophils, 1 per cent. The cells varied greatly in size and shape. There were many normoblasts, but no abnormal white cells. The Pirquet test was negative; the Wassermann test was 4 plus.

*Course.*—The patient was discharged to the polyclinic with a diagnosis of syphilitic anemia, and received intensive treatment for two years without any change in the general condition, the blood picture, or the size of the liver and spleen.

Fig. 3 (case 4).—Moderate mongoloid appearance.

In June, 1924, she was readmitted on the recommendation of the director of the polyclinic, who noticed her resemblance to patients 1 and 2. Since that time she has been under intermittent observation, in and out of the hospital.

The main features of the case have been as follows: She has constantly shown marked hemolysis, the blood serum being deeply pigmented, with positive indirect van den Bergh tests and icteric index as high as 25, while the urine has shown excessive urobilinogen, and at times increased iron content. Hemoglobinuria has not been detected as in case 5. She has no free gastric hydrochloric acid.

The urine is neutral or alkaline, and at times dark. It is at such times that an excess of iron is found.

The blood picture varies considerably. A characteristic count when the child was at her best was: hemoglobin content, 70 per cent; red blood cells, 4,208,000; white blood cells, 15,600; polymorphonuclears, 56.6 per cent; small lymphocytes, 20 per cent; large lymphocytes, 2.3 per cent; normoblasts, 14.6 per cent; megaloblasts, 0.3 per cent; azurophils, 2.3 per cent; unidentified, 1.3 per cent; eosinophils, 1.3 per cent; basophils, 0.6 per cent. Polychromatophilia and pronounced increase in reticulated forms are noted. No stippling was noted. Resistance to salt solutions had always been somewhat high, hemolysis beginning at about 0.35 per cent and being complete at 0.2 per cent. During the period of pronounced anemia the child had a blood calcium of 8, and phosphorus of 1.6. Later, these returned to normal.

Fig. 4 (case 1).—Appearance of skull at 11 months.

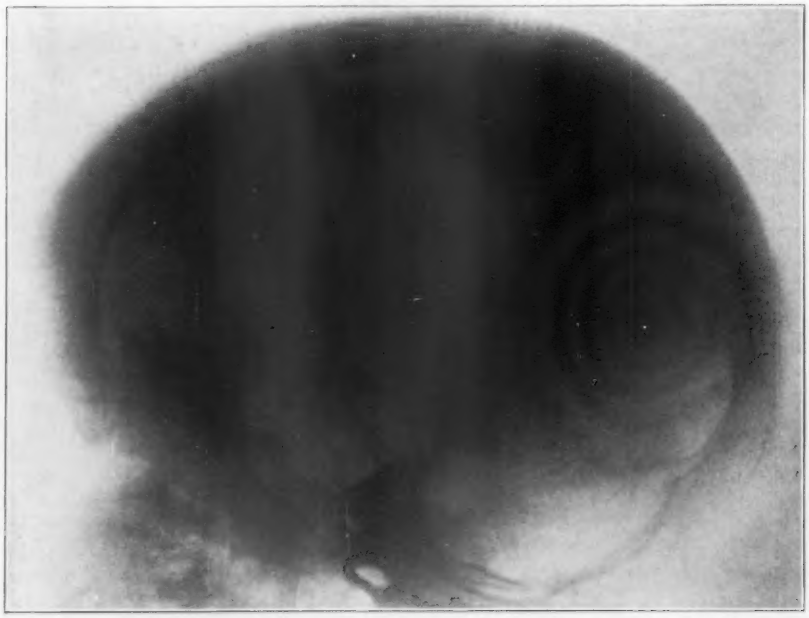


Fig. 5 (case 2).—Appearance of skull at 2 years and 9 months.

After the first 4 plus Wassermann reaction, numerous other tests were made at frequent intervals, and all were negative.

Although the bony peculiarities were not noted at the time of the patient's first admission, when looked for by inspection and by roentgen-ray examination, they were found to be definite, though not so extreme as in cases 1, 2 and 3. The skull, like that of patient 7, showed a deep groove along the sagittal suture, not like the deformities of rickets but more as if it were the result of thickening of the bones on each side.

The mongoloid appearance was pronounced in this case, though much less marked when the skin was comparatively clear.

The general condition varied with the anemia and the icterus. When the hemoglobin content was high and the skin was fairly clear, the child was bright and playful; at other times she was stupid and morose. The size of the spleen

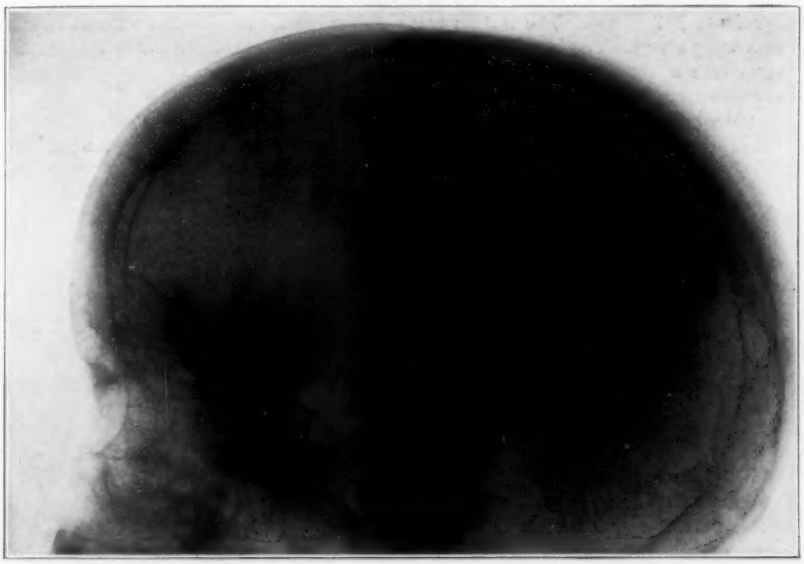


Fig. 6 (case 5).—Appearance of skull of Italian boy, aged 5 years.

varied greatly also, being barely palpable when she was at her best, and increasing rapidly with the fall of red cells and hemoglobin. However, she has never had what could be called "crises."

The most successful treatment in this case was an adequate anemia diet, plus the administration of inorganic iron and hydrochloric acid. While this was administered regularly at the hospital, the child improved steadily. She has not been given any transfusions. Splenectomy and roentgen-ray therapy of the spleen were discussed but were never advised. She was under observation at the same time that patient 5 was being studied after splenectomy, and seemed to make more rapid progress.

CASE 5.—*History.*—A. K., an Italian boy, aged 5 years, was brought to the clinic, Sept. 17, 1924, with the complaints of pallor, fatigue on exertion, abdominal enlargement and involuntary urination. The child's father had died of a rheumatic condition of the heart. Four other children were living and well. The mother was healthy, had had no miscarriages and had a negative Wassermann reaction.

The patient was born at full term; the delivery was instrumental. The weight at birth was 10 pounds (4.5 Kg.). The feeding history was excellent. The first dentition was at 8 months; he walked at 11 months and talked at 12 months. At the age of 2 years he had whooping cough, and at 4½ years diphtheria followed by enuresis.

The present illness seemed to have begun at about the age of 8 months, with pallor and abdominal enlargement, both of which persisted. Nothing else had been noted except weakness. He was admitted to the hospital, September 24. As in case 4, the facial resemblance to the other patients had been noted in the polyclinic, though in this boy the mongolian appearance was not so pronounced, as the cheek bones had not become so enlarged.

*Examination.*—The boy was short, plump, fairly well developed, bright and cooperative. The head was large and broad; the skin was dusky, and more yellow than the normal Italian coloring. The sclerae were slightly discolored. The cheek bones were prominent. The general appearance was noticeably similar to that of patients 1, 2 and 4. The tonsils were somewhat diseased. No enlarged lymph nodes were noted. The heart was normal, except for a soft systolic murmur. The lungs were normal. The abdomen was slightly distended. The spleen was palpable three fingerbreadths below the ribs and was smooth and firm. The liver was just palpable.

*Examination of the Blood.*—The hemoglobin content was 56 per cent; red blood cells, 4,170,000; white blood cells, 13,900; polymorphonuclears, 27 per cent; small lymphocytes, 69 per cent; large lymphocytes, 2 per cent; eosinophils, 2 per cent; many normoblasts; many vacuolated polymorphonuclear cells, anisocytosis and polychromatophilia; reticulated red cells, 10 per cent; bleeding time, one minute; coagulation time, seven and one-half minutes; fragility: hemolysis began at 0.35 per cent; it was complete at 0.2 per cent. Calcium and phosphorus were normal.

The Pirquet and Wassermann reactions were negative.

Roentgenograms of the skull and long bones showed changes similar to those in the other children and of about the same degree as those noted in case 4.

In the succeeding days more, but smaller, vacuoles were noted in the polymorphonuclears. There were numerous megaloblasts and a few myelocytes, and occasional primitive marrow cells were seen.

The urine was constantly alkaline and dark but contained no bile, while urobilinogen was found only once. From later developments, it is probable that the color was due to hematin.

The patient seemed to be losing ground, becoming rapidly weaker and more jaundiced, and on October 11 splenectomy was performed; no difficulties were encountered. No supernumerary spleens were found.

*Gross Examination* (Dr. Witwer).—The spleen was unusually large, being approximately twice the size of a normal adult spleen. It weighed 420 Gm. The capsule was distinctly thickened, wrinkled and adherent to the splenic substance. The spleen was firm, and on section the knife met with considerable resistance. Little blood escaped from the vessels, and on scraping the cut surface with the knife little of the splenic pulp was removed.

There was a diffuse, grayish-white discoloration, with small bands of firm tissue (apparently fibrous) coursing throughout the substance of the spleen.

The impression gained from the examination of the gross specimen was that the condition was one of chronic splenomegaly with extensive fibrosis, and a thickened and adherent capsule.

*Microscopic Examination.*—One was immediately struck with the extensive amount of fibrous tissue evident in the sections. The capsule was definitely thickened. The trabeculae were markedly hypertrophied. The malpighian bodies were relatively few and small. The tissue surrounding these structures was extensively fibrose. There was no evidence of pigment formation nor of myeloid or lymphoid metaplasia.

Under high power magnification, a few mononuclear eosinophilic cells were observed. These did not appear to be of myeloid origin. The staining qualities

of the cells of the stroma were not those of an actively proliferating, fibrous tissue. Few nuclear elements were demonstrated in the stroma. The blood vessels which were observed appeared to be of normal construction.

*Course.*—After the splenectomy, the boy was under close observation for about six months. Following splenectomy the great increase in nucleated red cells and the increased resistance to hemolysis described in similar cases were noted.[2] Six days after operation the normoblasts numbered 75,000, and reached a maximum of about 300,000, near which they remained for almost six months, when they decreased to a little less than 100,000. Hemolysis was only slight at 0.1 per cent. The jaundice diminished rapidly, but never entirely disappeared, and returned in some degree from time to time.

There was no increase in the anemia immediately after the operation; in fact, the red cells actually showed a temporary increase, reaching 5,000,000 on the eleventh day, but without a proportionate increase in hemoglobin. The red cells and hemoglobin soon decreased to about the level observed before the operation, and after that remained near that figure, the count running somewhat lower; however, the hemoglobin was about the same, the index having been raised.

Numerous detailed blood studies were made during the six months following the operation, the main features of which were the enormous numbers of normoblasts, with occasional megaloblasts, the constant leukocytosis of about 20,000, the large numbers (from 10 to 16 per cent) of reticulated red cells, and the occasional occurrence of myelocytes and other marrow forms. Stippling was marked at times, and occasionally a high percentage of azurophil lymphocytes was noted.

The blood phosphorus and calcium began to diminish soon after the operation, and in February reached low points of 1.56 and 2.5, respectively. A study of their metabolism was undertaken in March, but by this time the phosphorus had returned to normal. The study showed a pronouncedly negative calcium balance, while that of the phosphorus was slightly positive. Examination of the stomach had shown an absence of free hydrochloric acid, with considerable retention. Acid was administered, and following this the blood calcium returned to normal. No relation could be determined between the state of the anemia and the blood calcium and phosphorus.

The urinalysis was interesting. The urine was constantly alkaline and usually dark, sometimes much more than at others. Bile was never present, and traces of urobilinogen were found only occasionally. There was a constant increase in the iron content over normal, and when the color was intense the pigment could be recognized as alkaline hematin. It was especially dark during the days following transfusion.

The blood serum was pigmented; it showed a positive indirect van den Bergh reaction, and at times a reddish color and responded to tests for hemoglobin.

The stools were dark and contained urobilin in excess. The total pigment excretion in the urine and the stools was determined and found greatly increased.

The reaction to transfusion was interesting. The patient received two transfusions of 100 cc. each, which were followed by a slight increase in red cells and hemoglobin which lasted for only three or four days. The first was followed the next day by more myeloblasts than had been observed at any other time. The urine became dark after the transfusion, and contained a great excess of iron. Apparently the transfused blood was rapidly hemolyzed. The patient's serum did not show a hemolytic action in vitro on other blood, and careful cross agglutination tests were made before transfusion.

Various therapeutic measures, most of which were without effect, were tried while the patient was under observation. Sunshine, the quartz lamp, cod liver oil, iron in various forms and methods of administration and transfusion made no change. The boy first showed a gain in weight under the administration of hydro-

2. Stillman, R. G.: Von Jaksch's Anemia, Am. J. M. Sc. **153**:218 (Feb.) 1917. Pool and Stillman: Surgery of the Spleen, New York, D. Appleton & Co., 1923.

chloric acid, while the moderate gain in red cells and hemoglobin and the diminution of normoblasts, which appeared in the later observations, were coincident with the giving of mixed spleen and red bone marrow.

On the whole, the patient seemed to thrive fairly well after the operation; he was happy and lively, but we felt that we could not see any result from removing the spleen except the lessening of the jaundice. Hemolysis was evidently going on as before.

In the early summer of 1925, the patient's family moved to Los Angeles. We have heard from a clinic there that the boy is more anemic than when last seen here.

CASE 6.—(By courtesy of Dr. Kenneth Blackfan, from his clinic at the Children's Hospital of Boston.) *History.*—L. Z., a Greek boy, aged 2 years and 9 months, was admitted to the hospital, Dec. 6, 1925, with pallor and swelling of the abdomen for four or five months as the chief complaints.

Fig. 7 (case 6).—Appearance of skull of Greek boy, aged 2 years and 9 months.

The family history was wholly negative except that one brother died of anemia similar to the patient's at 1 year of age. The father, mother and five other children were living and well.

The patient's birth, feeding and development during the first year had been normal. His recent diet had been lacking in vegetables and meat. He had been constipated for six months. He had had pertussis (?) five months prior to examination, and had not been well since. Tonsillectomy had been performed three weeks before coming to the hospital. There had been no other illnesses.

*Present Illness.*—The patient had been "under par" and pale for five months; he had had abdominal swelling for four months, abdominal discomfort for three months, dyspnea for one month, and had been less active for three months.

*Physical Examination.*—On admission, a poorly developed and nourished, semistuporous child was seen. The skin was pale and of a yellow tinge. The general appearance was of oriental rather than of Greek descent, and was suggestive of cretinism.

General enlargement of the superficial lymph nodes, especially of the cervical lymph nodes, was present; all were discrete; none were tender.

The head and neck were normal except for a bulging forehead and visible pulsation of the vessels of the neck. The chest was normal except for a rapid heart beat with diffuse impulse and blowing, widely transmitted systolic murmur, with accentuated P-2.

The abdomen was enlarged and rounded, with bulging flanks. The spleen was palpable, extending to 2.5 cm. below the level of the umbilicus, with sharp and notched edge. The liver dulness extended from the sixth interspace in the anterior axillary line to 1¼ inches below the costal margin. There were no other observations of note.

The diagnoses considered were: von Jaksch's anemia; Banti's disease; Gaucher's disease; myelogenous leukemia; infectious endocarditis; congenital heart defect; malignant tumor of the liver or spleen; myeloma or chloroma.

Fig. 8 (case 2).—Appearance of bones of legs. The transparency of the tibia should be noted.

*Examination of the Blood.*—The hemoglobin content was 30 per cent; red blood cells, 2,072,000; white blood cells, 34,330; megaloblasts, 12,480; dividing megaloblasts, 480; normoblasts, 960; polymorphonuclears, 43.7 per cent; plasmocytes, 1.4 per cent; plasmoblasts, 0.4 per cent; myelocytes, 15 per cent; premyelocytes, 0.4 per cent; myeloblasts, 0.8 per cent; small lymphocytes, 24.1 per cent; large lymphocytes, 4.8 per cent; pathologic lymphocytes, 0.4 per cent; large mononuclears and transitionals, 4.8 per cent.

Anisocytosis was marked; poikilocytosis was present, but less marked. Many cells showed diffuse basophilia. An occasional one showed punctate basophilia. Howell-Joly bodies were rare; there were no Cabot's rings. Macrocytes and microcytes were fairly numerous. Some red cells showed moderate achromia; others stained well throughout. The platelets seemed diminished.

After a transfusion, the hemoglobin rose to 45 per cent and the red cells to 3,392,000. Otherwise the condition was not greatly changed. Before the transfusion the white cells reached 95,000 on one count.

The urinalysis showed nothing of importance. The Wassermann and tuberculin tests were negative.

*Roentgen-Ray Examination.*—On December 6, roentgenograms of the skull, chest, arms and legs showed peculiar structure of the bones; they were coarse and moth-eaten in appearance, apparently decalcified in part but without actual destruction. This was particularly noted in the scapulae, humeri, radii, ribs, clavicles and tibiae, and was not so marked in the skull. The appearance suggested the diffuse infiltration seen in leukemia.

*Pathologic Report.*—A small gland removed from the neck showed hyperplastic lymphoid tissue with many polymorphonuclears in the lymph channels. There was marked proliferation of the endothelium lining these channels. No evidence of leukemia or Hodgkin's disease was found.

On Feb. 14, 1926, the patient was seen in consultation by Dr. Minot. He reported: tremendous activity of the red cell elements of the marrow (all possible immature forms and many immature white blood cells of the myelocyte series consistent with von Jaksch's anemia). However, roentgenograms of the bones and the enlarged lymph nodes made him wonder whether this was not a condition resembling lymphoblastoma with the process involving the marrow, thus causing peripheral blood, or whether it was a form of leukemia per se. He did not advise splenectomy.

The patient's course in the hospital was uneventful. He had intercurrent measles and several attacks of epistaxis. He ate well and was fairly comfortable. He had only one transfusion, and the last blood count in the record showed a 40 per cent hemoglobin content, 3,195,000 red blood cells with 39,700 white blood cells. His physical condition was unchanged.

CASE 7.—*History.*—E. C., a mulatto boy, aged 18 months, was admitted to the Children's Hospital on Sept. 8, 1926, with the chief complaint of a lump in the left side, which had been noticed for six months, and which apparently was increasing in size. The father and mother were living. The father was asthmatic and the mother was not strong; they were in the South and no further history was obtainable. The child had been nursed for one month; since then he had had an apparently inadequate diet (largely condensed milk) until recently. Lately, egg, orange, liver, potato and cod liver oil had been added to the milk diet, but the orange and oil had been stopped on account of vomiting.

The patient had never been strong but had had no definite disease. His appetite had been poor and he had vomited often. The pallor and the swelling in the left side of the abdomen had been noticed for six months, with progressive weakness; there had been no other symptoms.

*Physical Examination.*—A blond mulatto child, poorly developed and nourished, was seen. The natural coloring of the skin would obscure any possible jaundice, but the sclerae were clear. There was generalized slight hyperplasia of the lymph nodes.

The skull seemed large and wide. The inner table was not quite closed at the fontanel, and there was a wide opening in the outer table. There was a decided groove along the sagittal suture, and the frontal bosses were prominent. The head otherwise was normal, except for decided pallor of the mucous membrane of the mouth.

The thorax was narrow, flaring somewhat below. There was moderate beading at the ends of the ribs. The heart and lungs were normal. The abdomen was slightly prominent, soft and tender. The liver was barely palpable. The spleen, which was smooth and hard, extended to just below the level of the navel and nearly to the midline. The extremities showed moderate epiphyseal widening. One testicle was undescended.

*Examination of the Blood.*—The hemoglobin content was 35 per cent; red blood cells, 3,200,000; white blood cells, 12,200; polymorphonuclears, 54 per cent; small mononuclears, 28 per cent; large mononuclears, 17 per cent; eosinophils, 1 per cent; normoblasts, 7; white blood cells, 40,100; platelets, 80,000. There was extreme variation in the size and shape of the red cells. Polychromatophilia was marked. There was 10 per cent of reticulated red blood cells. The serum was definitely pigmented. The direct van den Bergh test was negative;

the indirect test was positive. The icteric index was 8. The test for fragility showed that hemolysis began at 0.5 per cent and was complete at 0.35 per cent; control, 0.4 to 0.3 per cent. In the second examination, hemolysis began at 0.45 per cent, and was complete at 0.35 per cent; control, 0.42 to 0.35 per cent.

The urine contained an excess of urobilinogen but no bile. The Wassermann and Pirquet tests were negative.

Roentgen-ray examination disclosed that the skull was at least of twice its normal thickness and seemed porous. Definition in the roentgenograms was not good, owing perhaps to the deep groove. The long bones showed the same changes as seen in the other children, in moderate degree. There were also signs of some rachitic changes at the epiphyses.

This patient is under observation, with no other treatment than a diet for anemia. He is eating well and seems to be improving.

This child was the only one in the series who seemed to have had an adequate reason for a secondary anemia.

He differed from the others also in lacking the mongoloid facies. This seems to be because the bones of the cheek so far have not been involved in the bony thickening.

*Roentgenologic Studies* (Dr. Lawrence Reynolds).—Many roentgenograms have been made of the skulls and long bones of these patients, and the appearances noted have been constant, though varying in degree.

The cranial bones have all shown thickening, which in one patient (case 2) under observation progressed from about 0.75 cm. at 11 months to nearly 2 cm. at death. The thickening was limited to the medullary portion, while the tables seemed unusually thin. In the earlier stages and in the less severe cases, the marrow had a mottled, spongy appearance, not seen in roentgenograms of the normal skull, while in late stages there was a striking vertical striation, well shown in figure 5. This striation is explained by the increase of spongy, trabeculated bone found at necropsy in cases 1, 2 and 3.

The long bones also showed marked changes. The bones seemed somewhat wider than normal. The cortex was thin, and the bone was unusually transparent, as if lacking in lime. The medulla showed an abnormal amount of reticulation, corresponding again to the new growth of trabeculae found after death.

The ilia and scapulae also showed a marked fan-like striation. Such changes perhaps might be found in any disease in which overstimulation of the bone marrow occurred in early life, accompanied by insufficient lime deposit. We have, however, failed so far to discover them in other patients, with the single exception of roentgenograms received from Dr. Grulee of a patient with a diagnosis of sickle-cell anemia, in which the occipital bone especially showed thickening and vertical striation. The long bones did not give a characteristic picture. Quantitative chemical studies of the skull of patient 2 showed the various constituents to be within normal limits.

## COMMENT

These cases seem to belong to a fairly definite clinical group, though we must admit that our chain of evidence is not complete.

We should define them as a form of hemolytic anemia, developing in early life and dependent probably on some congenital defect in the hemolytopoietic system. Clinically, in some children the picture resembles that of von Jaksch's anemia which is accepted by those who believe it to be a real disease entity, in other children, it fits better into the large group of cases of atypical hemolytic jaundice. Cases 1, 2 and 3 seem more like von Jaksch's disease. They also have features strongly suggesting a form of leukemia, but the necropsy observations

exclude this definitely. The other four cases might be considered as atypical hemolytic jaundice.

We have taken up this question of classification in a paper on von Jaksch's anemia,[3] and we shall not discuss it in detail here.

In regard to individual features and our reasons for putting the cases in one group, we considered:

1. Evidence as to a congenital cause. With one exception, the disease seems to have been well advanced in all of these patients before the end of the first year, and the one who first showed symptoms at a little over 2 years had a brother who died in his first year of a similar condition. Only one patient (case 7) had what seemed a convincing reason for profound secondary anemia, unless we believe the dubious congenital syphilis to have been the etiologic factor in three of the cases, in spite of the total lack of result from thorough treatment.

If the cause is congenital, it is apparently not hereditary, though two families had two children affected.

2. The blood picture. The main points seem to be the striking evidence of marrow stimulation presented by the great number of immature forms; the constant leukocytosis, and the absence of increased fragility. Variations in the types of the white cells noted in different cases do not seem of especial importance. Case 1 did not show immature red forms, and these elements were less in evidence in all of the first three cases than in the others. The observations at necropsy explain this. Evidently when the patients came under observation, the erythropoietic marrow was already exhausted by prolonged overstimulation.

The absence in all cases of evidence of increased fragility is important.

3. The question of hemolysis. In cases 1, 2, 3 and 6, the blood serum and the stools were not studied for evidence of hemolysis. We do not consider the absence of increased urobilinogen at all conclusive. If the urobilin excretion is to be taken as the measure of hemolysis, a quantitative estimation of the stool must be made also, and this is not a simple process. Case 5 is one in point. We think that the skin pigmentation noted in all but case 3 is indicative of chronic hemolysis. The bone changes, too, we consider secondary to a hemolytic process. In the other cases, hemolysis was a constant feature. We have come to believe that for purposes of classification, the blood serum of all anemic patients should be studied for hemolysis by means of both the van den Bergh test and the icteric index determination, and that much confusion would be avoided by definite separation of hemolytic and nonhemolytic forms.

4. The changes in the bones. When we first observed these, we could find nothing similar described in the literature, and thought that

---

3. Cooley, T. B.: Von Jaksch's Anemia, Am. J. Dis. Child. **33**:786 (May) 1927.

we had stumbled on something peculiar to this group. More recently, however, Gänsslen,[4] in discussing a large group of patients with familial hemolytic icterus, speaks of the frequency of what he calls "Turmschaedel." He does not describe the skulls in detail, but the change may well be similar to what we have seen. One or two others have mentioned large heads in hemolytic icterus, and as has already been said, we have roentgen-ray evidence of the same appearance in "sickle-cell anemia," which, if it really is a disease entity, is also a form of hemolytic icterus.

Our explanation of these changes in the bones is that they are the result of the reaction of the marrow to prolonged overstimulation as a consequence of chronic hemolysis, beginning before the cortex is too firm to permit the overgrowth of marrow. In earlier stages and in less severe cases, the porous appearance in the roentgenograms seems to represent marrow hyperplasia, while in the terminal stages the pronounced striation indicates replacement of exhausted marrow by new bone, as found at the autopsies. That the bone change is not primary seems to be shown by the fact that the patient in case 2 had only slight indication when first seen, though the splenic enlargement was already marked.

Grulee's case and Gänsslen's observations prevent our thinking of these bone characteristics as peculiar to this group. We think, however, that we have good reason to believe them indicative of a chronic hemolytic process, belonging to the general group of hemolytic icterus.

With the roentgen ray, we have studied the skulls and long bones in many cases of nonhemolytic anemias and of rickets and syphilis, and have found no sign of any similar change.

5. The peculiar facial appearance. As the facial appearance is dependent on the combination of jaundice and changes in the skull, we do not consider it especially important; but it is so striking at times that we wonder that it has not been noted before. It might well be a feature of the classic type of congenital hemolytic icterus.

We have reported these cases mainly to call attention to the peculiar facies and the changes in the bones, readily demonstrable by the roentgen ray, in connection with a fairly constant blood picture. In a further paper we expect to discuss their classification, with respect to the present conceptions of von Jaksch's anemia and hemolytic icterus.

---

4. Gänsslen, M.: Hemolytic Jaundice, Deutsches Arch. f. klin. Med. **140**:210, 1922; Hemolytic Diathesis, ibid. **146**:1, 1924.

# ANTIRACHITIC PROPERTIES OF IRRADIATED DRY MILK*

G. C. SUPPLEE, Ph.D.
AND
ODESSA D. DOW, M.S.
BAINBRIDGE, N. Y.

The comparatively recent discoveries of Hess [1] and of Steenbock,[2] in which it was found that exposure to ultraviolet irradiation enhanced the antirachitic potency of certain antirachitically inactive substances, have been confirmed from other sources. Since milk is universally used in the infant dietary and because it is relatively ineffective as a specific for the prevention and cure of rickets, it is only natural that experimentation and clinical observations with irradiated milk should soon follow the discovery of the principle of activation. The reported clinical observations now available, even though limited, seem to agree that beneficial results accrue from the use of milk so treated.

Kramer [3] states that in a series of eight patients with active rickets the administration of irradiated milk produced healing in every case. Curative effects were observed at the end of the third week and were marked at the end of the fourth week. It was also observed that a greater retention of calcium and phosphorus resulted from feeding the irradiated milk. Cowell [4] found that after one month the roentgenograms of the wrists of children receiving 1 pint daily of irradiated milk which had been produced in the winter, showed decided improvement in calcification. Halac and Nassau [5] have shown that a high antirachitic value is imparted to raw milk by a brief period of irradiation. They assert that the rachitic condition of the children under observation was completely relieved in two or three weeks as a result of feeding irradiated milk. Mackay and Shaw [6] and György,[7] having used irradiated

*Received for publication, April 27, 1927.

*From The Research Laboratory of The Dry Milk Company, Bainbridge, New York.

1. Hess, A. F.: Experiments on the Action of Light in Relation to Rickets, Proc. Am. Pediat. Soc., June 7, 1924; abstr. in Am. J. Dis. Child. **28**:517 (Oct.) 1924.

2. Steenbock, H., and Black, A.: J. Biol. Chem. **61**:405, 1924.

3. Kramer, Benjamin,: Rickets in Infants, Am. J. Dis. Child. **30**:195 (Aug.) 1925.

4. Cowell, S. J.: Brit. M. J. **1**:594, 1925.

5. Halac, E. E., and Nassau, E.: Ztschr. f. d. ges. phys. Therap., 1926, vol. 31.

6. Mackay, H. M. M., and Shaw, H. F.: Brit. M. J. **2**:344, 1925.

7. György, P.: Klin. Wchnschr. **5**:747, 1926.

dry milk, asserted that it was a potent factor in curing uncomplicated rickets. The latter observes that once dry milk is irradiated it retains its full potency for long periods of time.

The antirachitic activation of milk to a degree that renders it a reliable prophylactic material for diets used in the prevention of rickets is a subject that presents manifold possibilities. Hess and Unger [8] and others quoted by them have come to the conclusion that 50 per cent or more of the children of the poorer classes are affected with rickets to a greater or less degree. The prevalence of the disease, therefore, warrants serious consideration of any prophylactic measures that may be readily adaptable for general application. Irradiated foodstuffs, and particularly milk, seem to suggest a source of greater potential benefit, easily obtained, than is to be expected by the now generally accepted procedures for combating the disease. The proved merits of cod liver oil, direct exposure to sunlight and the bodily exposure to the rays of the quartz mercury vapor lamp are known to be potent methods for the suppression of rickets, but universal application of these methods is of necessity restricted. Furthermore, the investigations of Steenbock and Black [9] indicate that a comparatively low level of the antirachitic factor extended over a long period of time may be preferable to a high level for only a short period of time. On the basis of these observations, the advantages of feeding infants a prophylactic dietary of irradiated milk over the relatively long period in which milk is fed is at once obvious.

The antirachitic fortification of milk to supply all bottle fed infants is a procedure that cannot be readily adapted for home use, nor is the procedure a practicable one for the majority of practitioners. Therefore, up to the present time the feeding of irradiated milk has been confined to hospitals and institutions in which equipment and personnel are available for the proper preparation of the product. Such limitations will of necessity prevent a wide dissemination of the benefits known to result from the use of activated milk and, unless the principle is applied to a suitable and easily accessible preparation, many infants will be deprived of a needed prophylactic of rickets. While irradiated dry milk has been prepared experimentally for clinical observations, it has been only recently that the principle of irradiation has been utilized for mass production of this product.[10] In the commercial production of antirachitically activated dry milk, certain objectionable features, which manifested themselves in the early experimental methods of

8. Hess, A. F., and Unger, L. J.: Seasonal Variations of Rickets, Am. J. Dis. Child. **22**:186 (Aug.) 1921.

9. Steenbock, H., and Black, A.: J. Biol. Chem. **64**:263, 1925.

10. The dry milk referred to is known as Dryco brand.

irradiation, appear to have been overcome. These objectionable features, namely, the development of a disagreeable taste and odor, and possible destruction of vitamin A, were undoubtedly due to the lack of recognition of certain factors now known to be important for the proper treatment of the product. The avoidance of over-exposure to the rays of short wave length, and the application of a perfected technic of irradiation has been intimated by Kramer [3] and appears to have been applied, on a limited scale at any rate, by Halac and Nassau.[5]

TABLE 1.—*Percentage of Ash in Long Bones of White Rats Fed Variable Quantities Of Irradiated and Nonirradiated Milk*

| Rachitic Ration with | 2 Cc. Daily | 4 Cc. Daily | 7 Cc. Daily | 9 Cc. Daily | 15 Cc. Daily |
|---|---|---|---|---|---|
| Nonirradiated Dry Milk | 43.55 | 45.55 | 47.29 | 52.80 | 55.61 |
| Irradiated Dry Milk | 49.00 | 53.07 | 55.18 | 58.22 | 60.09 |

TABLE 2.—*Comparative Antirachitic Properties of Irradiated And Nonirradiated Dry Milk* *

| Rat No. | Amount Reconstituted Dry Milk per Day (Cc.) | Treatment of Dry Milk | Per Cent Ash in Humeri | Roentgenograms | Costochrondral Junctions |
|---|---|---|---|---|---|
| 873 | 1 | Nonirradiated | 45.07 | Rickets marked | Much enlarged |
| 888 | 1 | Irradiated | 49.04 | Rickets moderate | Enlarged |
| 948 | 2 | Nonirradiated | 44.97 | Rickets marked | Much enlarged |
| 936 | 2 | Irradiated | 48.89 | Rickets slight | Slightly enlarged |
| 875 | 4 | Nonirradiated | 48.80 | Rickets slight | Slightly enlarged |
| 890 | 4 | Irradiated | 56.00 | Rickets negative | Normal |
| 847 | 4 | Nonirradiated | 42.65 | Rickets moderate | Enlarged |
| 859 | 4 | Irradiated | 52.77 | Rickets slight | Slightly enlarged |
| 927 | 4 | Nonirradiated | 45.85 | Rickets moderate | Enlarged |
| 942 | 4 | Irradiated | 53.32 | Rickets very slight | Slightly enlarged |
| 1037 | 4 | Nonirradiated | 43.55 | Rickets moderate | Enlarged |
| 1048 | 4 | Irradiated | 55.04 | Rickets trace | Normal |
| 881 | 9 | Nonirradiated | 54.14 | Rickets moderate | Slightly enlarged |
| 895 | 9 | Irradiated | 59.52 | Rickets negative | Normal |
| 851A | 9 | Nonirradiated | 54.84 | Rickets moderate | Enlarged |
| 865 | 9 | Irradiated | 60.29 | Rickets negative | Normal |
| 901 | 9 | Nonirradiated | 54.44 | Rickets moderate | Slightly enlarged |
| 1018 | 9 | Irradiated | 61.62 | Rickets negative | Normal |
| 1042 | 9 | Nonirradiated | 54.24 | Rickets slight | Slightly enlarged |
| 1055 | 9 | Irradiated | 59.98 | Rickets negative | Normal |
| 884 | 15 | Nonirradiated | 62.33 | Rickets negative | Normal |
| 900 | 15 | Irradiated | 62.43 | Rickets negative | Normal |
| 856 | 15 | Nonirradiated | 54.08 | Rickets slight | Normal |
| 867 | 15 | Irradiated | 63.03 | Rickets negative | Normal |

* These results were from different samples of the irradiated and nonirradiated dry milk obtained at intervals through a period of eighteen months.

## RESULTS FROM IRRADIATED DRY MILK

The dry milk to which reference has been made is a product desiccated by the revolving double cylinder process and contains 12 per cent of butter fat. Its antirachitic and calcifying properties are enhanced by exposing the product to the rays of the quartz mercury vapor lamp in a manner which permits practically the entire surface area of any given particle of milk solids to remain within the activating influence of the rays for a brief period, which is estimated to be approximately one minute. The degree of antirachitic potency and calcifying properties

imparted to this product is best determined by comparing the results obtained with the product before and after application of the method of irradiation to which it is subjected. The results of such comparisons are shown later in this paper. White rats were used for all comparative studies, and the laboratory methods were carried out according to standard and recognized procedures. Varying quantities of the irradiated and nonirradiated dry milk were fed in conjunction with a rachitic ration [11] for a period of forty-eight days, at the end of which time the long bones were analyzed for ash content, roentgenograms of representative specimens of each group were obtained,[12] and autopsies were performed on all experimental animals. In making the determinations of bone ash, the procedure recommended by Bethke, Steenbock and Nelson [13] was followed. The ash content of the bones, therefore, is expressed on the water and fat free basis.

From 219 individual comparisons with the irradiated and nonirradiated product fed under identical conditions, the results shown in table 1 were obtained. In table 2 are shown some of the results obtained with the irradiated and nonirradiated dry milk, using the ash content of the bones, the roentgenograms and the condition of the costochrondral junctions as the basis for comparison.

## VITAMIN POTENCY OF IRRADIATED DRY MILK

On the basis of preliminary experiments with irradiated milk, reports of which have been published to date, there has been some consideration of the possibility of destruction of vitamin A. Titus, Hughes, Henshaw and Fitch [14] claim that vitamin A is materially decreased in the irradiated milk. Their method of irradiation was to expose a layer of milk 2 mm. in depth at a distance of from 18 to 20 inches from the light. A personal communication from one of the authors states that the milk was irradiated for twenty minutes. Spinka [15] asserts that vitamin A is not destroyed by an exposure of twenty minutes to the ultraviolet rays but that the ozone generated by the lamp brings about detrimental results. He states that these results are not manifested when air is excluded from the product during irradiation. From these data, it would appear

11. Sherman, H. C., and Pappenheimer, A. M.: Proc. Soc. Exper. Biol. & Med. **18**:193, 1920-1921.

12. The roentgenograms were prepared and interpreted by Dr. A. F. Hess and Dr. Charles Gottlieb of New York.

13. Bethke, R. M.; Steenbock, H., and Nelson, M. T.: J. Biol. Chem. **58**: 71, 1923.

14. Titus, R. W.; Hughes, J. S.; Henshaw, W. R., and Fitch, J. B.: J. Ind. and Eng. Chem. **18**:843, 1926.

15. Spinka, J.: Biochem. Ztschr. **153**:197, 1924.

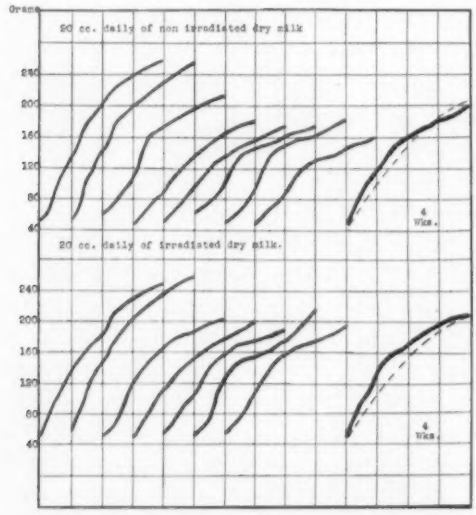



Fig. 1.—Growth curves of white rats receiving 20 cc. daily of irradiated and nonirradiated dry milk as the sole source of vitamin A. The results show that there is no impairment of vitamin A in the irradiated product. The curve at the extreme right is a composite curve for the group, compared with the normal curve.

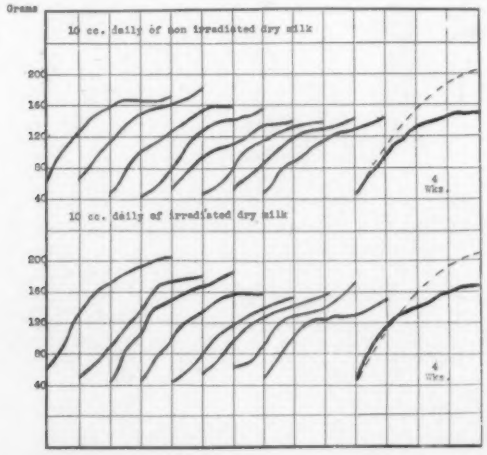



Fig. 2.—Growth curves of white rats receiving 10 cc. of irradiated and non-irradiated dry milk as the sole source of vitamin A. Even though 10 cc. of the irradiated or nonirradiated products is insufficient to furnish adequate vitamin A for normal growth, the results show that there has been no impairment of vitamin A in the irradiated product. The curve at the extreme right is a composite curve for the group compared with the normal growth curve.

that there is no definite proof that vitamin A is destroyed by irradiation per se. In order to determine whether vitamin A was destroyed in the dry milk irradiated with suitable precautions, several experimental studies have been conducted with the irradiated and nonirradiated product. Figures 1 and 2 show the growth obtained by feeding white rats 10 and

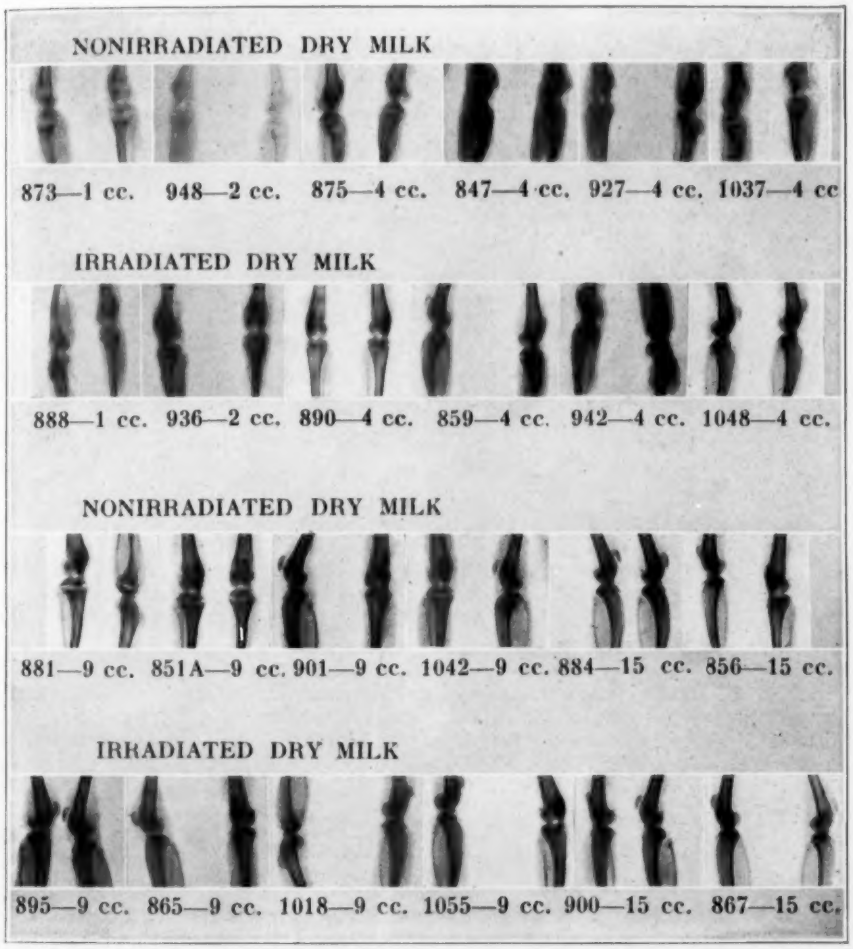

NONIRRADIATED DRY MILK
873—1 cc. 948—2 cc. 875—4 cc. 847—4 cc. 927—4 cc. 1037—4 cc
IRRADIATED DRY MILK
888—1 cc. 936—2 cc. 890—4 cc. 859—4 cc. 942—4 cc. 1048—4 cc.
NONIRRADIATED DRY MILK
881—9 cc. 851A—9 cc. 901—9 cc. 1042—9 cc. 884—15 cc. 856—15 cc.
IRRADIATED DRY MILK
895—9 cc. 865—9 cc. 1018—9 cc. 1055—9 cc. 900—15 cc. 867—15 cc.

Fig. 3.—Roentgenograms of joints of white rats which have received irradiated and nonirradiated dry milk.

20 cc. quantities daily of the treated and untreated dry milk as the sole source of vitamin A. From these results it appears that there is no impairment of growth due to decreased fat soluble vitamin content of the irradiated product. In fact, the composite growth curve for the respective groups shows that the irradiated product allows better growth than

the nonirradiated product. This result is presumably due to increased antirachitic properties. Further tests conducted with this product wherein the body store of vitamin A was first depleted by feeding a vitamin A free ration for from six to eight weeks showed that when either the irradiated or nonirradiated dry milk was fed in 5 and 10 cc. quantities daily, as the sole source of this factor, growth was resumed within a short time. The severe xerophthalmia that developed during the period in which vitamin A was not given was completely cured—in the majority of cases, within from ten days to two weeks. The fact that no distinguishable difference was observed in the results from irradiated and nonirradiated material indicates that the method of treat-

Fig. 4.—Ribs of white rats showing differences in costochondral junctions resulting from feeding irradiated and nonirradiated dry milk. *A*, after use of irradiated dry milk, showing normal costochondral junctions; *B*, after use of nonirradiated dry milk, showing enlarged costochondral junctions.

ment as applied to this product has not measurably affected its vitamin A potency. The foregoing studies were all conducted with milk produced in winter.

Since the oxidizing effects of ozone have been cited as detrimental to irradiated milk, tests were conducted to ascertain if such a result was manifested by destruction of vitamin C in the product under consideration. Eighty cubic centimeters of the reconstituted irradiated and nonirradiated dry milk were fed to guinea-pigs daily as the sole source of the antiscorbutic factor. The results showed that during an experimental period of sixteen weeks no symptoms of scurvy were manifested in the animals receiving either product. The animals in each group grew equally well, and autopsy revealed no significant pathologic conditions indicating unfavorable action by the irradiated product.

COMMENT

The favorable results obtained with dry milk irradiated with ultraviolet rays, from the standpoint of laboratory studies, indicate that nutritive and therapeutic properties of the product are enhanced to an appreciable degree. It appears that the beneficial results known to accrue to food products exposed to ultraviolet rays can be attained without measurable destruction of the readily oxidizable vitamins A and C, provided that a suitable technic of irradiation is used. Critical studies of the product under consideration have shown that there is no evidence of a disagreeable flavor and odor commonly found in milk products that are exposed to the ultraviolet rays for long periods of time. Furthermore, the usual keeping qualities of the product are apparently unimpaired. The irradiated product has been found to keep satisfactorily and apparently in its original condition for a period of several months. The comparative studies which have been made indicate that the process of activation as applied does not accelerate oxidation of the fatty constituents to a degree that impairs the nutritive value or in any way induces changes of a detrimental character.

# CIRRHOSIS OF THE PANCREAS AND LIVER IN AN INFANT*

CORNELIA DE LANGE, M.D.
AMSTERDAM, THE NETHERLANDS

In June, 1926, I [1] described the morbid anatomy in a case of diabetes in which the onset occurred at the age of 8 months. In this case, a normal pancreatic gland was found. The following case is worthy of description because it shows the opposite of this condition. I did not consider it a case of syphilis or of diabetes, and a pathologic examination afterward showed the typical characteristics of a diabetic pancreas.

## REPORT OF CASE

*History.*—A. was the third child of healthy parents; the other two children were healthy. The mother had not had any abortions. The child was born at term, but weighed only 2,650 Gm. The mother could say with certainty that the child was yellow on the seventh day; whether it was yellow before that she could not say definitely. The yellow tint never went away after the seventh day. The child was fed exclusively on the breast during the first four weeks, and after that on a mixed diet, partly on the breast and partly on buttermilk. It did not grow.

The urine was a deep yellow. In the third week the child had a rash, which disappeared again spontaneously after three weeks. At the age of 6½ weeks, the child was taken to the hospital. Then it weighed only 2,200 Gm. and appeared atrophic. No rash or skin cleavages were present. The skin was peeling badly, especially on the face and legs, and was seriously icteric. Nothing abnormal was discovered in the heart or the lungs. The liver had a sharp edge, protruding about 2 cm. below the costal border; the spleen also was palpable. The urine contained a great deal of albumin, not any sugar or urobilin, and much bile pigment. In the sediment, numerous red and white blood corpuscles, but not any cylinders were present. A blood smear showed: myelocytes, 2 per cent; polymorphonuclear neutrophils, 36.3 per cent; eosinophils, 2 per cent; basophils, 0; lymphocytes, 57.6 per cent; transitional forms, 3 per cent; Türk forms, 1 per cent. There was a displacement to the left (Arneth), and most of the polymorphonuclear neutrophils had a slight toxic granulation. Many lymphocytes showed vacuoles. Among the red corpuscles, anisocytosis and poikilocytosis and some red corpuscles with nuclei were present, while a small number of cells were polychromatophilic. No bleeding took place when a puncture was made with a needle. The child's condition was serious, and it died within forty-eight hours after coming into the hospital. The Wassermann test could not be performed.

---

* Received for publication, April 25, 1927.

* From the Emma Hospital for Sick Children.

1. De Lange, Cornelia: Morbid Anatomy in a Case of Diabetes, Am. J. Dis. Child. **31**:840 (June) 1926.

The stools were dyspeptic on the first day; they were firm on the second day, and not altogether colorless.

Section was carried out by Dr. J. C. Schippers six and one-half hours after death. The clinical diagnosis was: atrophy, icterus gravior.

The body of the infant was greatly emaciated and showed no cadaver rigidity but some cadaver spots. The subcutaneous fatty tissue had, for the most part, disappeared. When the abdomen was opened, a small amount of clear fluid was found. The liver was bronze colored; it had a sharp edge and reached 1½ finger-breadths below the costal border. Hydrops of the gallbladder was present. Pressure on the gallbladder caused bile to exude from the papilla vateri. The large bile ducts appeared normal and could be probed with a sound. The liver weighed 151.5 Gm. The liver on section was also bronze; the knife did not make a scraping sound in cutting the section, and yet on looking at it carefully, one had the impression that there was too much connective tissue. The normal liver marking could not be seen. The spleen was greatly enlarged; it had a violet color, weighed 15 Gm., and had a somewhat granulated surface. On section, the follicles could be seen. The measurements of the spleen were 60 by 35 by 20 mm.

The pancreas was large and hard, and weighed 13.5 Gm.

The appendix lay in a line with the cecum and did not show any adhesions. There was nothing special to note macroscopically about the kidneys and suprarenal bodies. When the thorax was opened, the following conditions were found: At the place of insertion of the diaphragm on the sternum a few enlarged lymph glands were present. No abnormalities of the heart were found. On both sides there was a fairly extensive paravertebral pneumonia. The left lung was imperfectly separated into its lobes. In both lungs were numerous subserous hemorrhages, while spots of atelectasis alternated with emphysema.

*Microscopic Examination.*—Sections were embedded in paraffin, and the following stains were used: hematoxylin-eosin, Mallory, Domenici, Best, Weigert and Levaditi.

Pancreas Body: There was a large increase of the connective tissue—interlobular as well as intralobular. The connective tissue was rich in round cells and fibroblasts. The round cells were all uninuclear; some had hardly any protoplasm edge, while others had more. A fair number of plasma cells and some mitoses were present. The excretory ducts showed nothing of importance. The blood vessels had fairly thick walls, but there was no endarteritis and no perivascular infiltration. The parenchyma was everywhere surrounded by connective tissue; in some places one could see small acini entirely isolated by it. Although the cell nuclei were everywhere well preserved, the parenchyma in many places has a shriveled up appearance. This might have been partly an artificial result, but also, in reality, it might be explained by the pressure of the connective tissue. The number of islands was not diminished, and the fact that many small and also so-called free islands were found is not unusual at this age. However, the fact that a large majority of the islands had an abnormal appearance was striking. Only a few of the islands showed cells regularly grouped so as to form little rods, and which were provided with abundant protoplasm. In many islands, the connective tissue was seen to be increased to a greater or lesser extent, while the cells had taken on the aspect of lymphocytes. The islands were mostly misformed, have irregularly distributed groups of cells, in places pressed up together toward the periphery. It was noticeable that sometimes the connective tissue of the periphery grew into an island, in which case the sclerosis did not develop from the pericapillary connective tissue.

In some places the acini lay so closely pressed against the islands that they almost appeared to be in them, and only external to them was connective tissue present. Such instances seemed to prove that the islands did not have definite capsules of connective tissue of their own. In almost every stain were found some islands showing hyaline degeneration, the cells of which had completely taken on the character of lymphocytes, thus showing the presence of the last stage of hydropic degeneration (figs. 1, 2, 3, 4, 5). Figure 6 shows for the sake of comparison, a normal island of average size in the midst of normal parenchyma.

Caput Pancreatis: More connective tissue was present here than in the body. Some islands were altogether sclerotic and were scarcely recognizable any more as islands. In others, one could see, here and there, a cell lying apart, while the

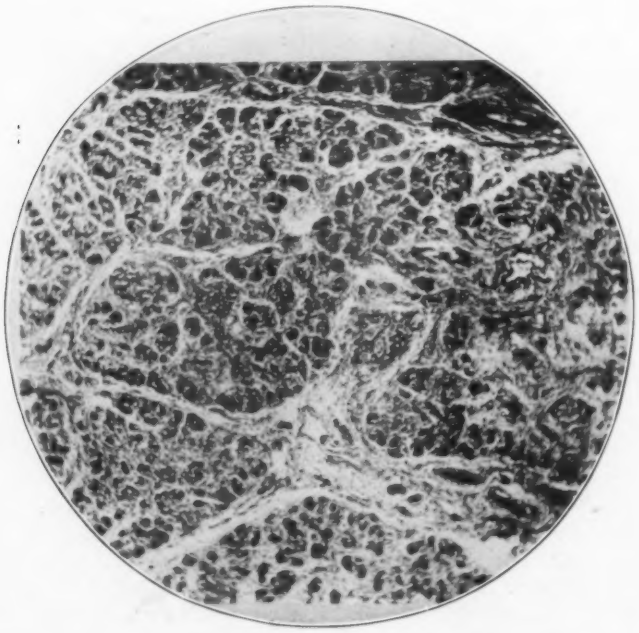


Fig. 1.—Appearance of cirrhotic pancreas.

other cells of the same island were clumped together into heaps. However, in fibrous parts were sometimes found strikingly well preserved islands, which seemed to prove that the insular apparatus possessed a certain amount of independence.

Cauda Pancreatis: In sections taken from this part were places in which there was less connective tissue and the construction of the gland as well as the islands seemed more normal, but in general, the same condition as described existed. In preparations taken from the tail, I saw in one place new formation of acini and in another place new formation of islands. In the interstitial tissue of the pancreas, no elastic fibers, such as have been described sometimes in cirrhosis, were seen. In the pancreas, no spirochetes could be discovered.

Liver and Spleen: The numerous bile thrombi and the dilated and twisted bile capillaries and the bile pigment in the liver cells, also the small bile ducts con-

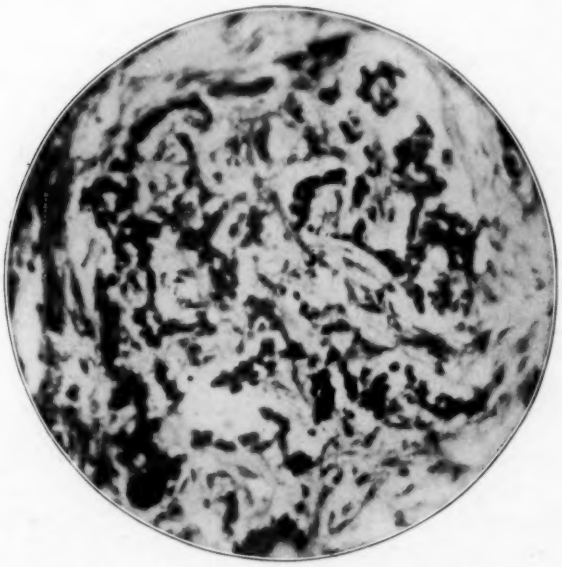


Fig. 2.—Large sclerotic island, with atrophic cells.

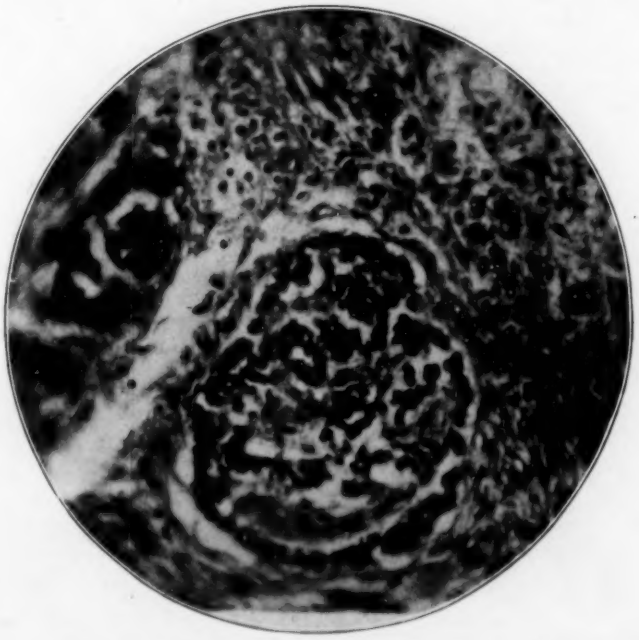


Fig. 3.—"Free" islet, with increased connective tissue.

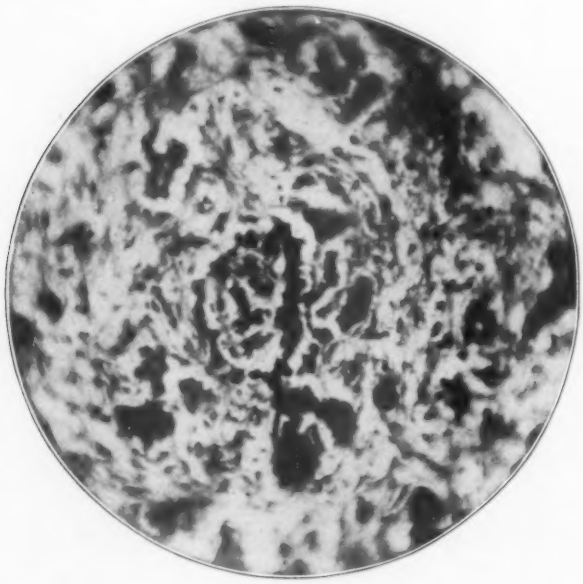


Fig. 4.—Misformed small island with irregularly distributed cells, of which only the nuclei are left.

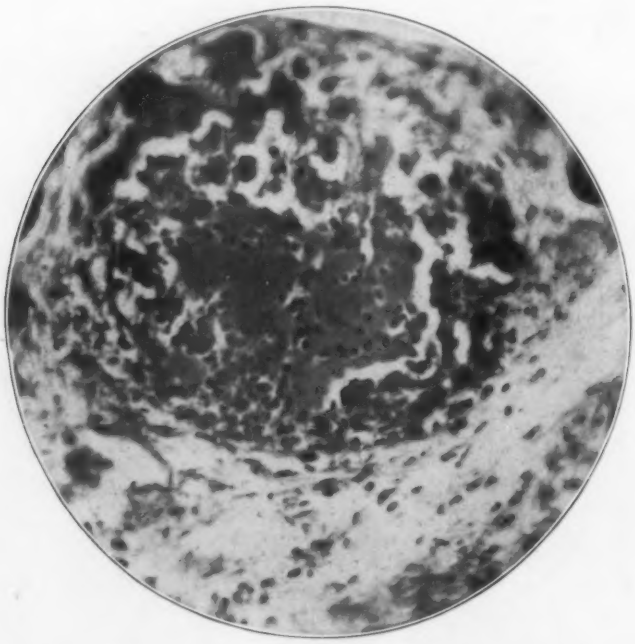


Fig. 5.—Hypertrophic and hyaline degeneration in an islet.

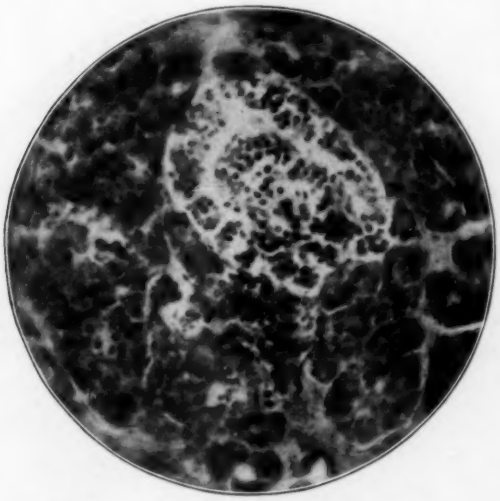


Fig. 6.—Normal middle-sized islet and normal parenchyma.

Fig. 7.—Appearance of liver, showing the interlobar connective tissue. High power magnification.

Fig. 8.—Appearance of liver. Low power magnification.

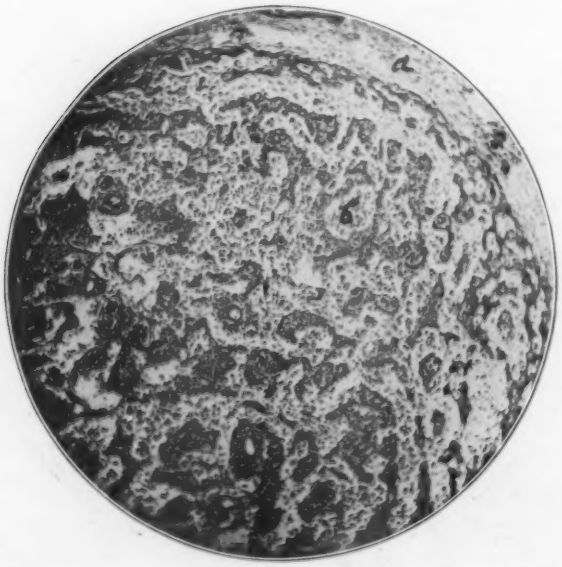



Fig. 9.—Lymph gland at the insertion of the diaphragm; (*a*) indicates the capsule; (*b*), lymph sinus with phagocytes.

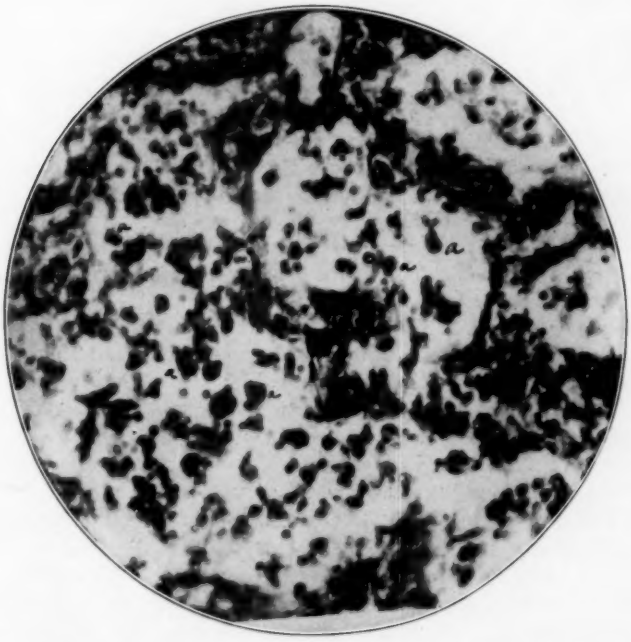



Fig. 10.—Lymph gland, showing the phagocytes (*a*) in the lymph sinus. High power magnification.

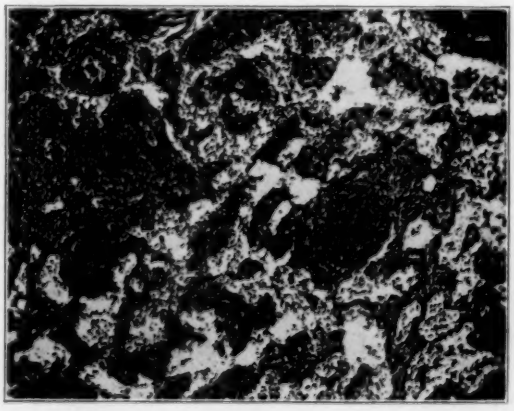


Fig. 11.—Lymph gland at the insertion of the diaphragm, showing hypertrophic medullary rays.

taining thrombi, proved that there had been a serious obstruction to the excretory flow of bile. The venae centrales were often difficult to distinguish; there was some irregularity in the construction of the liver. The parenchyma of the liver looked fairly normal; no regeneration could be seen. Giant cells were not present. There was an increase in the formation of connective tissue, chiefly interlobular, but also somewhat intralobular. The connective tissue was rich in monocytes No new formation of bile ducts had taken place. The blood capillaries were wide; they contained few red blood corpuscles, but many nuclear cells, resembling lymphocytes and here and there groups of or single myelocytes. At intervals in the bends of the capillaries were small embryonic formations of blood. No spirochetes could be found. The formation of connective tissue in the pancreas was much more marked than in the liver (figs. 7 and 8).

The spleen was hyperemic; the follicles were not marked. The connective tissue was somewhat increased. No pigment could be seen and almost no phagocytosis. The suprarenal bodies showed no thickening of the capsules. In the cortex, too much connective tissue was seen. No spirochetes were found.

The kidneys looked somewhat hyperemic. There were a few red and white blood corpuscles in Bowman's capsule. No leukocytic infiltrations and no gummas were seen around the blood vessels (cuffs). The mucous membrane of the pelvis was somewhat infiltrated. Glycogen was not present in Henle's loops.

*Lymph Glands at the Insertion of the Diaphragm.*—These glands showed a peculiar alteration. The so-called "Sekundärknötchen" in the cortex were only slightly noticeable and in some places were altogether absent. The medullary rays were hypertrophic. The lymph sinuses at the periphery as well as elsewhere were strikingly wide and contained, besides lymphocytes, a specially large number of large phagocytic monocytes, which had sometimes invaginated five or six small lymphocytes within their cell bodies (figs. 9 and 10). The endothelium of the sinus, when still attached to the wall, showed the same thing. Smear preparations of the bone marrow (femur diaphysis) appeared normal.

## COMMENT

I am of the opinion that, if one examines the origin of these pathologic alterations, one has to deal with a congenital process. The child was strikingly yellow on the seventh day of life, perhaps even before that. The activity of the reticulo-endothelial apparatus greatly increases after birth, causing a larger formation of bile and thus explaining why the icterus was not at once evident at birth. If one presupposes that the cirrhosis of the liver was congenital, then one may formulate a similar prognosis with regard to the cirrhosis of the pancreas, which was much more marked than in the liver. If one considers the case as one of congenital abnormality, then there is no reason to consider it as a case of diabetes. Clinically, there is no proof of it and no glycogen was found in the loops of Henle at the pathologic anatomic examination. It may be noted that in Bossert's [2] description of a case of nonsyphilitic cirrhosis of the liver in an infant, a serious glycosuria was present and the islands of Langerhans appeared absolutely normal.

2. Bossert, O.: Monatschr. f. Kinderh. **14**:174, 1916.

The task of proving the acceptability of my opinion, that the child was not suffering from syphilis, is more difficult. One is accustomed to associate an enlarged liver and spleen in an infant with syphilis. And, in spite of the strong and absolutely sound protest of the experienced Hochsinger,[3] one still looks on icterus as an argument in favor of syphilis. As far as my experience goes, Hochsinger is right, when he says that jaundice does not occur in hereditary syphilitic infants born at term. The more pediatricians study the pathologic anatomy of infancy, the more cases they will find of nonsyphilitic hepatosplenomegaly. This is my firm opinion.

Clinically, the diagnosis of atrophy, icterus gravior, was made in this infant, because there was nothing in the habitus of the child that made one think of syphilis. Three weeks after the death of the child, a Wassermann test was done on the mother, and a valuation of $+ \frac{4}{10}$ found according to the terminology of the quantitative method of Sormani. Usually this valuation $+ \frac{4}{10}$ is not considered of much importance clinically; at most, it causes some doubt as to the presence of syphilis, if there are clinical symptoms present as well. Such symptoms were absent in this case; the mother was healthy, had healthy children and had never had an abortion.

I agree, that, microscopically, abnormalities were found which might be an argument in favor of syphilis, and yet I think there was more against than for it: First, the fact that no spirochetes were found, in spite of a long search for them in the liver, pancreas and suprarenal bodies; second, that infiltrations round about the blood vessels were not found anywhere, these symptoms being typical of congenital syphilis, especially in the kidneys.

All authors agree that changes in the blood vessels of the kidneys are always present in cases of congenital syphilis, if the children have lived some weeks or months.[4] Cirrhosis of the pancreas has often been found in congenital syphilis, and the changes that one finds there have been explained as the result of an arrested development of the pancreas caused by the spirochetes (Kimla [5] and Seyfarth [6]). In the development of the pancreas, the excretory ducts are first formed, out of these. the islands, and from these the tubules should develop.

---

3. Hochsinger: Studien über die hereditäte Syphilis, Vienna, F. Deuticke. 1898, p. 321.

4. Queslier: Les néphrites interstitielles de hérédo-syphilis, Thèse de Paris. 1920.

5. Kimla, R.: Wien. M. Wchnschr. 1905, no. 31 and the following numbers.

6. Seyfarth, C.: Neue Beiträge zus Kenntnis der Langerhans-Inseln in menschlichen Pankreas u. ihre Beziehung zum Diabetes mellitus, Jena, 1920, quoted by Nakamura (footnote 7).

Although I believe, that Nakamura [7] has shown with sufficient certainty, that the islands as well as the acini develop from the epithelium of the duct, it is certainly a striking fact that in a syphilitic cirrhosis of the pancreas the insular apparatus is almost always found intact and the development of acini seriously hindered. This points to an earlier development of the islands than of the parenchyma of the glands.

In my case, it was the islands of Langerhans that were seriously affected, and this is therefore against its being of syphilitic origin. The islands of Langerhans showed the abnormalities that one otherwise encounters only in serious diabetic patients (hyaline and hydropic degeneration). In newly born children, one normally finds in the kidneys a few hyaline glomeruli, and one is inclined to think that this degeneration of the islands, at least to some extent, may have originated in utero. It should be mentioned that Nakamura found much alteration in the islands in three out of six patients having congenital syphilis which he examined, in one case a homogenization of the connective tissue being present.

The simultaneous occurrence of cirrhosis in the liver and pancreas has often been observed in adults. I may refer to the studies of Lando [8] and Poggenpohl.[9] In twenty-two cases of atrophic and in two of hypertrophic cirrhosis, the latter always found an intralobular sclerosis of the pancreas; in almost every case it had begun at the excretory ducts. For that reason he called the process a perisialangitis chronica and believes, partly as a result of experiments on animals, that the cause is a catarrh spreading up from the intestinal canal. This conception of the cause of cirrhosis is certainly not generally accepted.

Poggenpohl believes that the islands of Langerhans possess greater power of resistance than the rest of the tissue of the pancreas.

Lando found more alteration in the islands, but these were not serious either in intensity or in extent. In three cases in which hyaline degeneration was found, diabetes also was present.

The curious appearance of the lymph glands found at the insertion of the diaphragm at the sternum deserves attention. It was different from that found in an acutely or chronically inflamed lymph gland. One might speak of an overgrowth and increased activity of the endothelium. A certain amount of phagocytosis is always present, but in this case it greatly exceeded the normal amount. If one accepts the view of Heringa and Ten Berge [10] of the unity of connective tissue

7. Nakamura, N.: Virchows Arch. f. path. Anat., 1924, p. 253.
8. Lando, D. M.: Ztschr. f. Heil, 1906, vol. 27.
9. Poggenpohl: Virchows Arch. f. path. Anat., 1909, p. 196.
10. Heringa, G. C., and Ten Berge, B. S.: Nederl. Tijdschr. v. Geneesk **1**:1211, 1924.

and endothelium, then evidently here also an irritating agent has affected the connective tissue. It is a pity that no more lymph glands were examined.

I am inclined to explain this case as follows: During pregnancy, toxins produced by the mother had led to a disturbance in the balance between the tissues, causing a disproportionate growth of connective tissue in various organs. This connective tissue was not only young, but was also pathologic. It seems to me improbable that these alterations have been caused by spirochetes for the reasons mentioned in the foregoing.

In regard to the state of the pancreas, one must take into account that during the first few months of life, there are two sorts of cells to be found in the islands of Langerhans, showing the as yet imperfect differentiation. In the middle were large cells with translucent protoplasm, usually in the typical rodlike arrangement. Toward the periphery, the cells were smaller with dark protoplasm and lay close together. They look like atrophic cells, but the latter have still less protoplasm and their boundaries not so well defined (Nakamura). When this is taken into account, the majority of the islands must be considered as pathologic. Thus, normal pancreas in a serious case of diabetes and a greatly altered pancreas, when no diabetes was present, are described. Both observations point in the same direction and lead one to believe that, to use the terminology of neurology, the insular apparatus is not the primary but the secondary neuron.

Lately, there has been an increased number of reported cases of nonsyphilitic cirrhosis of the liver in infants. I have reported two cases,[11] and I have been impressed by a number of cases of congenital cirrhosis of the liver, in which other congenital abnormalities were present at the same time. In Bossert's [2] case there was also present a congenital cataract; in one of my two published reports of cases, a situs viscerum inversus was described and, in a case that I saw later on, mongolism was also present. All this points to intra-uterine disturbances.

Finally, it is of importance to report that Nakamura found a pancreas, which altogether resembled that found in congenital syphilis, in a large infant born at term, with chondodystrophia foetalis. This observation proves that other unknown causes also may lead to such a condition and is in line with my conception of the case reported in this paper.

---

11. De Lange, C.: Monatschr. f. Kinderh. **14**:351, 1916.

# TALIPOMANUS

## A REPORT OF THREE CASES IN ONE FAMILY *

EDGAR E. MARTMER, M.D.
DETROIT

Talipomanus or, as it is more commonly known, club hand, is one of the less common congenital deformities. The three cases reported are of interest since they occur in a mother and her two children.

Club hand is considered to be due to an interference with the development of the first ray and results in the absence or partial absence of the radius, carpal bones and thumb. All three of these cases show this interference in various degrees.

### REPORT OF CASES

CASE 1.—E. M., a well developed, well nourished child of 5 years, was seen, Feb. 25, 1926, suffering from scarlet fever, and presenting marked deformities of both forearms and hands. There was a total absence of both thumbs, the rest of the hands appearing normal. The wrists were flexible, and the carpal bones could not be felt. The radius and ulna of the right hand were palpated and felt intact, but the left radius was represented by a small bit of bone at the elbow joint. The ulna was markedly bowed. The roentgenogram (fig. 1) confirmed this examination, showing total absence of the bones of the thumbs. Four ossification centers were present in the right wrist and three centers in the left wrist.

CASE 2.—R. M., aged 7, a brother of E. M., was well developed and well nourished, and presented a similar deformity. The right hand showed a total absence of the thumb, total absence of the carpal bones, and a bowing of the ulna, associated with a hypoplasia of the radius. The left hand showed a total absence of the thumb and carpal bones. The radius was slightly shortened but otherwise was not deformed.

CASE 3.—Mrs. R. M., aged 35, the mother of the two children, was sensitive regarding her deformity, and would not allow roentgenograms to be made. However, examination showed a total absence of both thumbs; the carpal bones of the right hand could not be palpated, and the radius was represented by a short bit of bone, measuring about 2 inches (5 cm.) at the elbow joint. The ulna was curved similar to the bowing observed in the children. The left hand was intact except for the thumb, but the carpal bones could not be palpated. The radius was shortened and extended from the elbow joint for about 4 inches (10.16 cm.). The ulna was bowed, although not so markedly as in the other forearm. The mother, despite her deformity, was able to do most of her own work and to feed and clothe herself.

Both children were able to feed and clothe themselves.

### COMMENT

These cases are of interest not only because of the deformity but also because they show its transmission from the mother to both children.

---

* Received for publication, April 1, 1927.

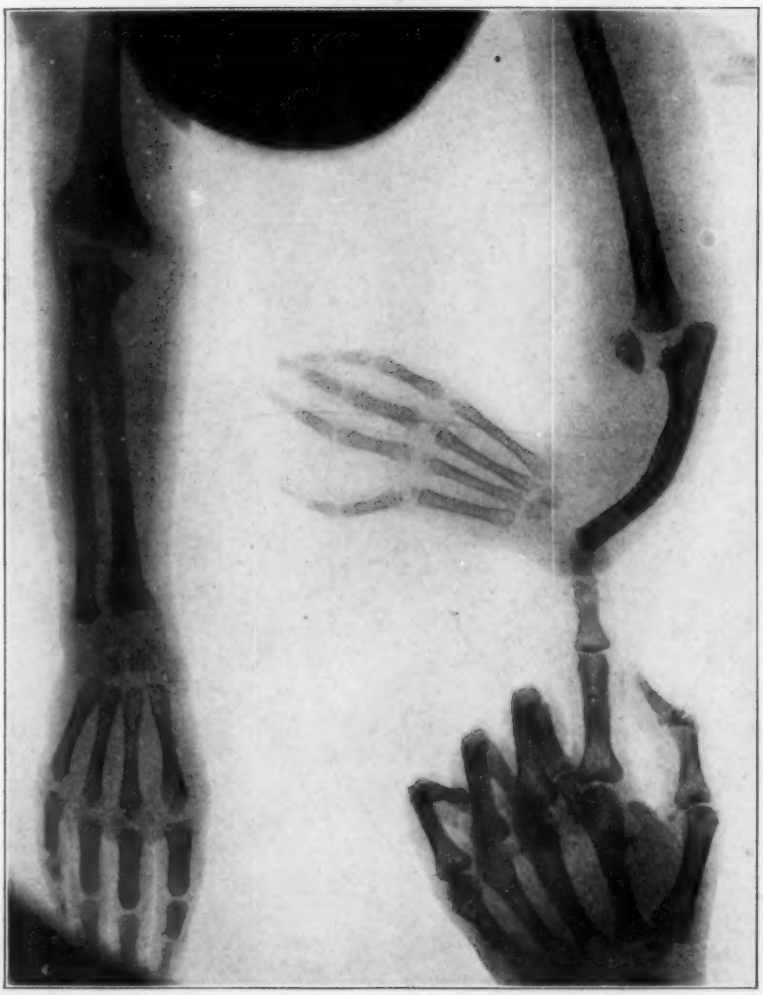


Fig. 1 (case 1).—Total absence of both thumbs in case of talipomanus.

Fig. 2 (case 2).—Similar condition in brother of patient in figure 1.

The question of operative intervention in these cases justly belongs to an orthopedic surgeon. Various methods of bone transplanting have been tried with varying degrees of success.

Specialized training would undoubtedly help these children to become useful citizens as they grow up.

1249 David Whitney Building.

# RICKETS

## AN UNUSUAL ROENTGENOGRAPHIC MANIFESTATION *

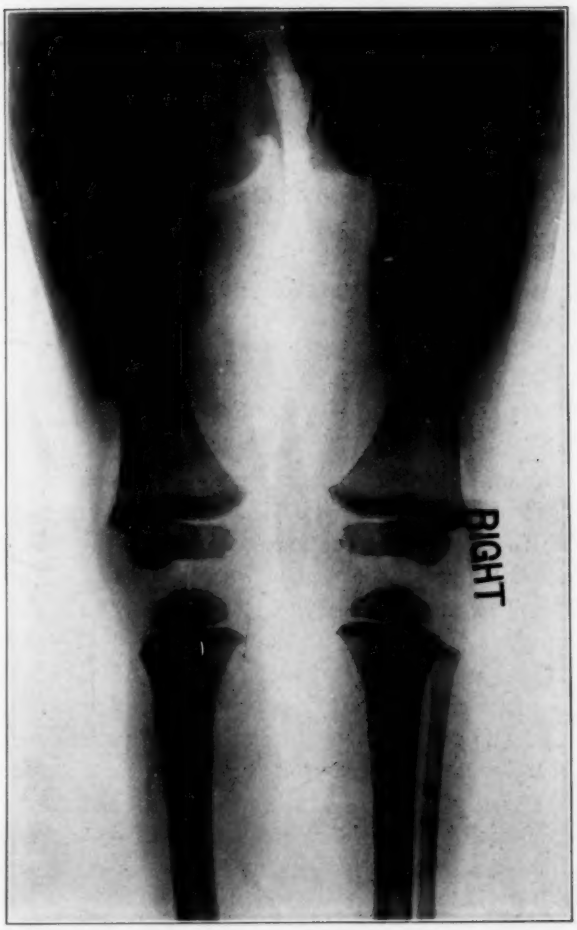
PHILIP LEWIN, M.D.
CHICAGO

The accompanying illustration is of interest because of the unusual roentgenographic shadow of the epiphyses, which present the appearance of an epiphysis within an epiphysis. This phenomenon is explained on the basis of a two-stage growth of the epiphysis.

### REPORT OF CASE

A white child, aged 2½ years, was referred by Dr. Julius Hess because of genu valgum. The only significant points in the history were as follows: He was a premature infant by four weeks and was breast fed for three and one-half months. At the age of 5 months, he developed a severe eczema which persisted for seven months and precluded the administration of orange juice, tomato juice, etc. He had an antipathy toward eggs. He was given cod liver oil and phosphorus from the fourth to the twenty-first months. Its administration was then discontinued for three months, when it was resumed. The physical observations of interest were moderate genu valgum and pronated feet.

* Received for publication, April 4, 1927.




Striking calcium-phosphorus effect on diaphyseal side of epiphyseal line plus epiphyseal shadow within epiphysis, indicating two stages of growth. (Roentgenogram by Dr. Hollis E. Potter.)

# THE HEART AND BLOOD VESSELS IN CONGENITAL SYPHILIS*

IRVING MATUSOFF, M.D.
AND
PAUL D. WHITE, M.D.
BOSTON

Serious cardiovascular disease, chiefly affecting the aorta, is a well known late complication of acquired syphilis. The rôle played by congenital syphilis in the production of cardiovascular disease is much less known and has received but scant attention in the literature. The desire to determine more definitely what immediate and remote effects congenital syphilis may have on the heart and aorta has stimulated the study presented herewith.

## REVIEW OF LITERATURE

### A. MYOCARDIAL CHANGES

In a book issued in 1885 by J. Parrot [1] "La syphilis héréditaire et le rachitis," reference is made to Rosen who in 1860 mentioned gummas of the heart in congenital syphilis. M. Wagner [2] observed myocarditis in a new-born infant whose mother had signs of syphilis. Virchow [3] found interstitial myocarditis and white hepatization in an 8 months' fetus. The mother undoubtedly had syphilis, and she had aborted four times previously. In 1875, Coupland [4] presented to the Pathological Society of London the viscera of a child who died from syphilis at the age of 3 months. The heart, more involved than any other organ, showed many small gummas which on microscopic examination gave the cellular infiltration reaction between the muscle fibers and the arterial walls.

In 1893, Mracek [5] found four cases of cardiac involvement in babies with congenital syphilis, two presenting a nodular or gummatous form and two a diffuse interstitial myocarditis.

---

* Received for publication, April 27, 1927.
*From the Cardiac Clinic of the Children's Hospital, and the Cardiac Clinic of the Massachusetts General Hospital.
*Read before the Heart Symposium of the Massachusetts General Hospital, Feb. 18, 1927.

1. Parrot, J.: La syphilis héréditaire et le rachitis, Paris, G. Masson, 1886, p. 69.
2. Wagner, M., cited by Parrot (footnote 1, p. 69).
3. Virchow, R., cited by Parrot (footnote 1, p. 70).
4. Coupland, S., cited by Parrot (footnote 1, p. 70).
5. Mracek, F.: Die Syphilis des Herzens bei erworbener und ererbter Lues, Arch. f. Dermat. u. Syph. **137**:279, 1893.

In 1896 Hektoen [6] reported a case of focal interstitial myocarditis in an infant of 6 weeks, of rather a nodular or gummatous form, the type that may cause sudden death.

Adler [7] demonstrated two cases of diffuse fatty degeneration of the myocardium due to congenital syphilis.

Warthin [8] observed that myocardial involvement in congenital syphilis is not uncommon, but that gummas are rare because the cellular infiltration is irregularly diffuse rather than circumscribed, and central caseation is not present.

In 1912, the same author [9] noticed a localization of the spirochetes in the heart muscle in congenital syphilis in the absence of any histologic lesions or spirochetes elsewhere. He reported two cases, one in an infant aged 3 months and one in an infant of 8 days. In both were seen degeneration of the muscle fibers, epithelial degeneration and cellular infiltration. In the Levaditi preparation these areas showed numerous spirochetes.[10]

Johannsen [11] states that he believes that myocarditis in congenital syphilis is not rare. Clinically, it may cause evident organic lesions. Sudden death may occur. He quotes two cases in which he considers that the end was caused by the myocardial involvement due to syphilitic infection. These are reported with detailed autopsy results.

In Pfaundler and Schlossman's work,[12] Hochsinger says, "In interstitial myocarditis the tissue between the muscle fibers shows cellular infiltrations. In the chronic forms callosities are frequently found which may lead to chronic aneurysms of the heart and sudden rupture. Here also belong the syphilitic callosities and gummata in the later stages of hereditary syphilis." Winogradow [12] found important pathologic anatomic changes in the automatic ganglions of the heart in twenty-two cases of congenital syphilis of infants. With interstitial growth of the connective tissue and changes in the blood vessels, severe degeneration of the ganglion cells has frequently been found. B. Fisher [12] described serious syphilitic changes in the myocardium with aneurysmal dilatation of the conus in a boy, aged 5 years.

---

6. Hektoen, L.: Foci of Interstitial Myocarditis in Syphilis, J. Path. & Bact. **3**:372, 1895.

7. Adler, I.: Observations on Cardiac Syphilis, Tr. A. Am. Phys., May 3, 1898, p. 73.

8. Warthin, A. S.: Congenital Syphilis of the Heart, Am. J. M. Sc. **141**: 398, 1911.

9. Warthin, A. S., and Snyder, E. J.: Localization of Spirochetae Pallidae in Heart Muscle, J. A. M. A. **58**:689 (March 9) 1912.

10. In a personal communication to the authors, Dr. A. S. Warthin states that he is convinced that congenital syphilis plays an important part in later cardiovascular disease.

11. Johannsen, N.: Congenital Syphilitic Myocarditis. Acta Pediat. **3**: 419, 1924.

12. Hochsinger, I.: Diseases of Children, trans. ed. Pfaundler & Schlossman, Philadelphia, J. B. Lippincott Company, 1912, vol. 3, pp. 508 and 516.

### B. ENDOCARDITIS DUE TO CONGENITAL SYPHILIS

Only infrequently have endocardial lesions been reported in congenital syphilis.

In 1898, Adler [7] described two cases of syphilitic endocarditis with endarteritis in various branches of the left coronary artery.

In 1908. Landois [13] reported an autopsy done on a girl, aged 6 years, which disclosed syphilitic endocarditis.

Hochsinger [12] says "Syphilitic endocarditis also occurs in children." "Arteriosclerosis, lead poisoning, and diabetes mellitus do not play any part in the occurrence of valvular lesions in childhood. Only syphilitic affections of the endocardium sometimes lead to heart lesions in childhood."

### C. VALVULAR LESIONS CAUSED BY CONGENITAL SYPHILIS

1. *Aortic Regurgitation.*—Haussman [14] reports three cases of aortic regurgitation which he believes were due to congenital syphilis. He bases his assumption on the fact that the patients had a diastolic murmur at the aortic area, with a normal pulse pressure and a history of no rheumatism. In our opinion, however, the rheumatic type of valve lesion is much more likely than the syphilitic with such findings. We have seen rheumatic cases with slight aortic valvular involvement and normal pulse pressure; these in later years sometimes developed the classic picture of well marked aortic regurgitation.

2. *Aortic Stenosis.*—Stoll,[15] in 1914, in his observations of late hereditary syphilis, states that he has seen several cases in which there were lesions of the aortic valve, and in four of which he found a positive luetin or Wassermann reaction. He mentions two patients in particular: One, a boy, aged 14, had a marked systolic murmur loudest at the right side of the base of the heart, without anemia; his mother, sister and brother gave positive Wassermann reactions. The other, a woman, aged 21, had pain between the shoulder blades, more severe on the left side, a systolic murmur at the second cartilage and a positive reaction, as had her mother. The condition cleared up with specific treatment. It is our opinion that these signs do not mean aortic stenosis, and certainly not syphilitic aortitis.

3. *Pulmonary Stenosis.*—This lesion was demonstrated with the spirochetes in a case reported by A. Mikhailovski [16] in an infant, aged 1½ months.

---

13. Landois, F.: Syphilitic Endocarditis, Arch. f. Dermat. u. Syph. **90**:221, 1908.

14. Haussman, T.: Congenital Syphilitic Insufficiency of the Aorta, München. med. Wchnschr. **72**:2093, 1925.

15. Stoll, H. F.: The Late Manifestations of Inherited Syphilis, J. A. M. A. **63**:1558 (Oct. 31) 1914.

16. Mikhailovski, A.: Thèse de Paris, 1913-1914, p. 131.

4. *Mitral Stenosis.*—In the discussion of Stoll's article,[16] R. N. Willson demonstrated two cases of marked mitral stenosis in which there was no history of any form of rheumatism, and in both cases the child and at least one of the parents were syphilitic. In one of these cases there was a ruptured aneurism of the thoracic aorta (in a child, aged 4).

Rarely it is possible that mitral stenosis may be of congenital origin; it is generally rheumatic; syphilis has not been proved to play a part.

### D. INVOLVEMENT OF THE AORTA

The real work in syphilitic aortitis began when Heller in 1899 pointed out the etiologic basis of acquired syphilis with regard to aortic disease. Since then, similar changes have been looked for in cases of congenital syphilis.

In 1905, Wiesner[17] investigated the aorta of ten syphilitic infants whose ages varied from several hours to several weeks. In nine cases he found thick infiltrates in the adventitia and media that consisted of lymphocytes, leukocytes and epithelial cells, and connective tissue proliferation. Seventeen cases of infants who died from birth trauma or acute infections, and were free from syphilis, served for controls. In no one of these latter cases was a picture found similar to that in the infants with congenital syphilis.

Wiesner's observations were confirmed by Bruhns.[18] In a series of eight syphilitic infants, Bruhns found changes in six similar to that described.

In 1907, Klotz[19] described a distinctive case of syphilitic arteritis of the aorta and pulmonic artery. He found hemorrhages in the media, cellular infiltration in the capillaries between the adventitia and the media and penetrating connective tissue swellings composed of giant cells from the adventitia to the media.

In the same year (1907) Wiesner and Rach[20] further confirmed these observations. They studied two series of cases: one series of eight nonsyphilitic infants and another of nineteen syphilitic infants. In the first series disease was not found; in the second series, they found changes in the aorta in sixteen of the nineteen infants similar to that described by Wiesner in 1905. In four of the latter cases they demonstrated the spirochetes in the heart and blood vessels.

---

17. Wiesner, J.: Syphilis of the Aorta, Centralbl. f. allg. Pathol. u. path. Anat. **16**:822, 1905.

18. Bruhns, C.: Ueber Aortenerkrankung bei Congenitaler Syphilis, Berl. klin. Wchnschr. **43**:217, 1906.

19. Klotz, O.: A Case of Congenital Syphilitic Aortitis, J. Path. & Bact. **12**:11, 1908.

20. Rach, E., and Wiesner, R.: Wien. klin. Wchnschr. **20**:521, 1907.

Waterman,[21] in 1908, noted aortitis in a case of hereditary syphilis. He concluded that congenital syphilitic aortitis shows itself first in the tunica adventitia and also that hereditary syphilis can cause an aneurysm.

Hochsinger [22] reported syphilitic aortitis in two children, one aged 8 years, and the other, 11.

In 1912, Rebaudi [23] investigated the aorta of seventeen syphilitic fetuses in the sixth to tenth months of pregnancy and found abnormal histology in thirteen aortas, which coincided with the changes of syphilitic aortitis. In one case he noticed a definite swelling of the wall of the aorta caused by infiltration and connective tissue formation. In five of the cases he found spirochetes.

In 1914, Veeder and Jeans [24] presented in their series a case of syphilitic aortitis.

In 1914, Stoll,[15] in his observations on inherited syphilis, reported three cases of aortitis, two of which were negative to the roentgen ray, and the third showed aortic dilatation.

Stolkind,[25] in 1920, states that he was unable to find spirochetes in the aortas of children over 2 years old.

In 1922, F. Thoenes [26] examined the aortas of ten infants who died from syphilis and of three patients who died from nutritional disturbances. In three of those with syphilis he found small-celled infiltrations in the vasa vasorum, in the adventitia, and in the blood vessels of the boundary line between the adventitia and the media. The cells consisted mostly of lymphocytes and epithelioid cells. Between the elastic fibers were seen vacuolated areas, in some of which the described cells were found. As a result, the wall was thickened. In some places the internal membrane showed proliferation of the connective tissue and here and there it seemed disintegrated into small particles.

Cesa-Bianchi [27] found spirochetes in the large vessels and heart muscle of twenty children. Sebrazès and Dupérié [28] found the organisms of syphilis in the aorta and pulmonary artery of a 10 day old infant.

---

21. Waterman, N.: Aortitis Syphilitica, Zentralbl. f. inn. Med. **29**:910, 1908.
22. Hochsinger, I.: Diseases of Children, trans. ed., Pfaundler & Schlossman, Philadelphia, J. B. Lippincott Company, 1908, vol. 3, p. 520.
23. Rebaudi, S.: Die Aortitis bei Congenitaler Syphilitischer Kindern, Monatschr. f. Geburtsh. u. Gynäk. **35**:681, 1912.
24. Veeder, B. S., and Jeans, P. C.: Diagnosis and Treatment of Late Hereditary Syphilis, Am. J. Dis. Child. **8**:283, (Oct.) 1914.
25. Stolkind, E. J.: Hereditary Syphilitic Aortitis, Brit. J. Child. Dis. **17**: 126, 1920.
26. Thoenes, F.: Syphilitic Aortitis in New Born, Ztschr. f. Kinderh. **33**: 113, 1922.
27. Cesa-Bianchi, D., cited by Stolkind (footnote 25).
28. Sabrazès, J., and Dupérié, R.: Syphilis of the Aorta, Arch. d. mal. du. coeur. **2**:257, 1909.

### E. ANEURYSMS OF EARLY LIFE

Le Boutellier [29] reported, in 1903, a series of fifty-nine cases of aneurysm in children, of which seventeen were located in the thoracic aorta, five in the abdominal aorta, four in the pulmonary artery, five in the femoral artery, two in the heart itself and the rest in miscellaneous arteries.

As to the causes of these aneurysms, in two there were definite histories of syphilis, three were of rheumatic origin, ten seemed to be due to various infections and the others were given as traumatic, congenital deformities of unknown origin. (It must be remembered that these cases were reported years before pathology and serology were on the definite footing they are on now.)

Since the above publication, in 1907, Willson and Marcy [30] reported a case of ruptured aneurysm in a young congenital syphilitic patient. The family history and appearance of the child allowed a diagnosis of congenital syphilitic aneurysm, which was confirmed at autopsy.

In 1919, Heiman [31] reported a case of aneurysm of the ascending arch of the aorta in a boy of 13 with a positive Wassermann reaction. The diagnosis was confirmed by roentgen ray, fluoroscopy and physical signs.

In addition, Bronson and Sutherland [32] have reported in children two cases of aneurysm due to congenital deformities and two cases of ruptured aneurysms, one traumatic and the other probably syphilitic.

In the literature there is thus a total of sixty-five aneurysms of different arteries in childhood. If one considers the report by Longcope,[33] in which he states that syphilis is responsible for most aneurysms, then it can reasonably be assumed that some of the aneurysms of miscellaneous origin in the foregoing series were probably of syphilitic origin.

### F. GENERAL ARTERIOSCLEROSIS

Osler [34] has stated that in congenital syphilis, diffuse or localized sclerosis of the arteries may occur sometimes early and sometimes as a late manifestation of syphilis hereditaria tarda.

---

29. Le Boutellier, T.: Aneurysm of Aortic Arch, Am. J. M. Sc. **152**:778, 1903.
30. Willson, R. N., and Marcy, A.: Rupture of an Aortic Aneurysm in a Child of Four Years, Tr. Coll. Phys. Phila. **29**:48, 1907.
31. Heiman, H.: Aneurysm of Ascending Arch in Boy of Thirteen, Arch. Pediat. **36**:543, 1919.
32. Bronson, E., and Sutherland, G. A.: Ruptured Aortic Aneurysm in Childhood, Brit. J. Child. Dis. **15**:241, 1918.
33. Longcope, W.: Syphilitic Aortitis: Its Diagnosis and Treatment, Arch. Int. Med. **11**:15 (Jan.) 1913.
34. Osler, W., and McCrae, T.: Modern Medicine, Philadelphia, Lea & Febiger, 1913, vol. 4, p. 453.

In 1908 Fremont-Smith [35] collected 144 cases of arteriosclerosis in the young, of which five were syphilitic in origin.

Genevrier [36] has stated that congenital syphilis may cause hypertension without cardiac or renal involvement. It becomes manifest about the eighth or tenth year, with anemia, retarded development and impairment of the general health.

### G. INVOLVEMENT OF PERIPHERAL VESSELS

Barlow [37] in 1877 was the first English author who described syphilitic changes in the blood vessels and choroiditis in an infant nearly 7 months old.

Ranke [38] found spirochetes in the cerebral vessels in nine of twelve congenitally syphilitic patients.

Berghinz [39] reported the case of a boy, aged 12 months, with a positive Wassermann reaction, who had edema of both lower limbs. At autopsy syphilitic arterial changes were found in the vessels below the popliteal space.

Bosanyi [40] reports a patient 18 months old with symmetrical gangrene of the right hand and both feet that cleared up with one course of arsphenamine. The treatment was then stopped, and in six months the trouble recurred; the lesions once again disappeared under arsphenamine treatment which was faithfully continued, and the condition did not then recur.

Lisser [41] collected twenty-two cases of Raynaud's disease associated with congenital syphilis. He thinks that 10 per cent of the cases of gangrene may be due to the syphilis itself.

Dupérié [42] reports five cases of Raynaud's disease, one of which was due to syphilitic endarteritis and cleared up rapidly under specific treatment.

Hahn [43] concluded from a study of 150 cases of congenital syphilis that a large majority of cases with vascular neurosis are due to the infec-

---

35. Fremont-Smith, F.: Arteriosclerosis in the Young, Am. J. M. Sc., new series, **135**:199, 1908.
36. Genevrier, J.: L'hypertension artérielle infantile stigmata de hérédosyphilis, Bull. méd. **39**:169, 1925.
37. Barlow, T., cited by Stolkind (footnote 25).
38. Ranke, K. E., cited by Stolkind (footnote 25).
39. Berghinz, G.: Symmetrical Gangrene of the Feet in Hereditary Syphilis, Pediatria **29**:301, 1921.
40. Bosanyi, A.: Raynaud's Disease as a Symptom of Hereditary Syphilis, Jahrb. f. Kinderh. **78**:177, 1913.
41. Lisser, H.: Syphilis and Raynaud's Disease, Arch. Int. Med. **16**:509 (Oct.) 1915.
42. Dupérié, R.: Syndrome de Raynaud, Gaz. hebd. d. sc. med. de Bordeaux **44**:411, 1923.
43. Hahn, L.: Cardiac and Vascular Lesions in Congenital Syphilis, Brit. J. Child. Dis. **19**:208, 1922.

tion, as are the serious cases of vascular crises in various regions of the body. The site of the disease is in the vessels, the vasomotor center or the endocrine glands, closely connected with the blood pressure.

In 1912, Lucas [44] stated that the arteries of the arch of Willis are attacked in congenital syphilis. Gummatous endarteritis of some of the large arteries in the brain or obliterative endarteritis of the small blood vessels of the brain may occur.

## SUMMARY OF LITERATURE

### PATHOLOGY OF THE HEART AND BLOOD VESSELS IN CONGENITAL SYPHILIS

*Heart.*—A diffuse myocarditis due to the presence of the *Spirochaetae pallidae* in large numbers has been found ordinarily without the production of characteristic macroscopic changes; thus, the presence or absence of involvement can only be revealed by a thorough microscopic examination of the myocardium. Parenchymatous degeneration of the heart muscle may occur, beginning with fatty degeneration, followed by atrophy and necrosis. The muscle fails to take the eosin stain properly. Interstitial myocardial changes may be found with vascular and perivascular infiltration of lymphocytes, plasma cells, epithelioid cells and fibroblastic proliferations. Spirochetae pallidae are sometimes found in great numbers.

*Aorta.*—The morbid changes in the aorta consist of cellular infiltration around the vasa vasorum in the adventitia, with involvement of the media. The vasa vasorum in the adventitia and media may be partially or completely obliterated and a growth of interstitial tissue ensues. The infiltration of cells consists of mononuclear, lymphocytic and epithelioid cells. This may result in connective tissue proliferations, with weakening of the elastic wall and aneurysm.

*Peripheral Vessels.*—Syphilitic conditions of the smaller blood vessels occur either as an obliterative endarteritis due to a proliferation of the subendothelial tissue which may fill the lumen or as nodular gummas in the adventitia of the artery.

Stokes [45] in his recent extensive work on syphilis has written as follows concerning the late visceral changes in congenital syphilis:

> In spite of the supersaturation of the patient with organisms before birth, the early involvement of the spleen and liver in a large proportion of cases, the fibrosis that affects to a greater or lesser extent the pancreas and the ductless glands, and the enormous numbers of spirochetes which are demonstrable in such tissues as the myocardium, the tardive heredosyphilitic patient presents very

44. Lucas, W. P.: The Wassermann Reaction in Syphilis: A Résumé of Current Literature, Am. J. Dis. Child. **3**:259 (April) 1912.

45. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia and London, W. B. Saunders Company, 1927.

little in the way of cardinal symptoms from the visceral and vascular structures. He has in fact, conquered or subdued his infection, and survived the fibrosis which it has induced. The liver and spleen are enlarged in only a slightly larger proportion of cases than in late acquired syphilis. I have seen only one really huge spleen in my experience, in a twelve-year old girl. The stomach and intestine have more than the relative immunity of acquired syphilis. The cardiovascular system, while occasionally the site of myocardial changes, only very rarely presents clinically recognizable aortitis.

## PRESENT INVESTIGATION

### A. RESULT OF AUTOPSY OBSERVATIONS

In studying 2,500 consecutive autopsy records at the Massachusetts General Hospital, we have found twenty cases that were diagnosed anatomically as congenital syphilis. In the first 800 autopsy protocols of the Infants' and Children's Hospital, Boston, we have found fifteen cases of congenital syphilis. These two groups total thirty-five cases in which all the patients were children.

In fourteen of the entire thirty-five cases (40 per cent), some pathologic changes due to syphilis were manifest in the heart or blood vessels, or both. A summary of these observations is as follows:

CASE 1.—The myocardium showed mononuclear leukocytic cells near and in the smaller blood vessels.

CASE 2.—The myocardium showed occasional mononuclear cells near and in the adventitia of some of the blood vessels. *Spirochaetae pallidae* were demonstrated.

CASE 3.—Grossly, the right ventricle seemed unusually dilated. The myocardium was pale red. Microscopically, edematous changes with areas of focal necrosis which had undergone fibrous tissue repair were seen.

CASE 4.—*Spirochaetae pallidae* were found in the heart muscle, which was "pale and flabby."

CASE 5.—Macroscopic examination was negative. Microscopic examination showed in the heart muscle nearest the pericardium a diffuse infiltration of wandering cells in the stroma tissue. Most of these cells were mononuclear, some endothelial and some lymphoid. No spirochetes were observed.

CASE 6.—In the heart muscle many *Spirochaetae pallidae* were demonstrated, but the cellular reaction was not marked. The child had received two sulpharsphenamine treatments before death.

CASE 7.—The myocardium was pale with areas of pinkish brown. There were also areas of atrophy and a moderate degree of necrosis.

CASE 8.—On the posterior wall of the left ventricle and the anterior wall of the right ventricle, two firm areas about 2.5 by 1.5 cm. were found, pale and of increased resistance. On section the walls in these places showed about one and one-half times the thickness elsewhere. The tissue was firm, homogeneous, somewhat glistening, yellowish gray and presenting the appearance of uncooked white meat of chicken. The valves and cavities were negative. The coronaries were small. Microscopically the myocardium showed the bundles of muscle fibers separated by clefts in which were fibroblasts, more or less loosely scattered, and some fibrillary substance. *Spirochaetae pallidae* were found in great numbers.

CASE 9.—Examination of the heart showed in many places infiltrations of mononuclear cells in the walls of the blood vessels. The muscle showed some fatty degeneration and areas of atrophy.

CASE 10.—Pyknotic polymorphonuclear cells and many mononulear cells were seen on the epicardium. The heart muscle beneath this showed the presence of numerous wandering cells of the lymphocytic group. There was a widespread vacuolization of the muscle fibers.

CASE 11.—In the heart were found areas of localized interstitial myocarditis with small-celled infiltration of the small blood vessels. In the aorta there was cellular infiltration of the vasa vasorum of the adventitia and those of the media. In one place a giant cell was noted.

CASE 12.—The myocardium showed perivascular and vascular infiltration of small cells of the lymphocytic, epithelioid and plasma cell type. *Spirochaetae pallidae* were seen in the heart muscle and in the blood vessels.

CASE 13.—The adventitia of the aorta and its boundary with the media showed small-celled infiltration which consisted mainly of lymphocytes. *Spirochaetae pallidae* were seen there in moderate number.

CASE 14.—In an infant, aged 2 months, the heart appeared to be somewhat enlarged. Little epicardial fat was seen. The muscle was pale. The pulmonary artery was opened in situ, and contained a postmortem blood clot, but was apparently normal. The ductus arteriosus was closed. The foramen ovale was also closed.

The aorta showed the intima at one place slightly thickened with vacuolization. Included in the section were several peri-aortic lymph nodes which were considerably congested. In their sinuses were many eosinophils and eosinophilic myelocytes. With the Levaditi stain several small areas were found in the adventitia of the aorta in which numerous *Spirochaetae pallidae* were present.

### SUMMARY OF AUTOPSY RESULTS (FOURTEEN CASES)[46]

*Spirochaetae pallidae* seen:

In the heart muscles—five times.
In the blood vessels—twice.
In the aorta—twice.
Total cases showing *Spirochaetae pallidae*—seven.

Disease demonstrated:

In the heart muscle—nine times.
In the blood vessels—five times.
In the aorta—three times.
Total cases showing disease—thirteen.

No cases of aortic regurgitation or of aneurysm were noted in our series. It is unfortunate that the aorta was not examined more often.

### B. CLINICAL STUDY

We have examined twenty-five congenital syphilitic patients of different ages and at different stages of treatment. In studying these patients, we were particular to bear in mind the observation of Gesteira,[47] who found an exaggerated aortic second sound in children with congenital syphilis, and also the observation of the

46. It is of interest that in our thirty-five cases we found the foramen ovale patent in eleven cases and the ductus arteriosus patent in ten cases.

47. Gesteira, M.: The Aorta in Congenital Syphilis, abstr., J. A. M. A. **85:** 1435 (Oct. 31) 1925.

Beretervide brothers [48] who state that the diameter of the ascending aorta is by roentgen ray about 1.3 cm. in healthy children, but wider and with a denser shadow in syphilitic children. They made these observations by orthodiagraphy of the aorta in 463 children with congenital syphilis and compared them with the observations in healthy children. They go so far as to state that if the aorta appears wider or denser than normal they treat the children for syphilis. In eight of our cases we obtained teloroentgenograms of the heart and aortic region with this point in mind.

In none of the twenty-five cases was there proof or even strong evidence that the heart muscle, valves, pericardium or aorta showed damage clinically which could be attributed to the syphilitic infection alone though some of the evidence was suggestive. The difficulty of interpreting murmurs in a congenital syphilitic patient who has passed through childhood diseases makes it impossible to arrive at definite conclusions clinically, but a loud aortic second sound in a patient with congenital syphilis should arouse suspicions of cardiovascular involvement. Twelve cases of our series of twenty-five showed some abnormal cardiovascular sign, often slight, as follows: (1) aortic second sound loud; (2) systolic murmur midway between the sternum and the apex, or at apex; or (3) definite enlargement of the heart was noted.

None of the roentgen-ray reports of the heart and aorta of our series showed characteristics similar to the observations made by the Beretervide brothers, i. e., aortic changes.

To illustrate the difficulty of ariving at definite conclusions clinically we shall report three cases with abnormal signs from our series of twenty-five.

CASE 1.—*History.*—R. F., a boy, aged 12 years, had not presented snuffles, paralysis, deformities or convulsions at birth. The mother had a positive Wassermann reaction. The boy had not had scarlet fever, influenza, sore throats, rheumatic fever, chorea or pertussis.

*Present Illness.*—At the age of 10 years, he became lame, and both knees were swollen. The local physician diagnosed the case as arthritis. Two months later the swelling of the knees recurred and the boy was admitted to the hospital. Here a positive Wassermann reaction was noted. During his stay in the hospital he developed interstitial keratitis. It was found on examination of the heart that the midclavicular line was 7 cm. from the midsternum and that the left border of dulness extended for 7.6 cm. Retromanubrial dulness was 5.5 cm. wide. The aortic second sound was louder than the pulmonic second. This was checked by three physicians. No murmur was present. The precordium was bulging and the apex beat diffuse. A roentgenogram of the heart showed a slight prominence high on the left border. Roentgen-ray measurements of the heart were: midsternum to the right border of the heart, 3.5 cm.; midsternum to the left border of the heart, 7.5 cm.; total transverse diameter, 11 cm.; internal diameter of the chest, 23 cm., and great vessels, 5.5 cm. The electrocardiogram showed sinus arrythmia. A roentgenogram of the long bones indicated syphilitic periostitis.

48. Beretervide, E. A., and Beretervide, J. J.: Aortitis in Children, abstr., J. A. M. A. **85**:1339 (Oct. 24) 1925.

*Comment.*—In this case, the family history of syphilis, positive Wassermann reaction and roentgen-ray observation of syphilitic periostitis made the diagnosis of congenital syphilis certain. The accentuated aortic second sound suggested aortic involvement in the absence of hypertension, but otherwise there was not any proof of it. The involvement of the knees may have been syphilitic in origin or due to a complicating polyarticular rheumatism, which at this age and in this climate is exceedingly common.

CASE 2.—*History.*—R. M., a boy, aged 5 years, had not had any sore throat, rheumatism or chorea. He had had scarlet fever, without any sequelae at an unknown age.

*Present Illness.*—About eight months before admission (at the age of 3 years, and 4 months), he began to limp, and to complain of pain in the right knee, which became tender and swollen. The left knee next became involved, and then both ankles. His temperature was normal. For a time his condition improved, but two months before admittance to the hospital he again started to limp and complain of pain in his right ankle. He was admitted to the hospital with a diagnosis of rheumatism. The right border of cardiac dulness extended 1.5 cm., and the left border dulness 7.5 cm. from the midsternum. The apex was in the fifth space. There was a soft blowing systolic murmur at the apex transmitted upward where it was again well heard at the base. The Wassermann reaction was positive.

A roentgenogram of the heart (after twelve treatments with sulpharsphenamine) revealed: midsternum to right border, 3.6 cm.; midsternum to left border, 7.2 cm.; total, 10.8 cm.; internal diameter of the chest 19 cm., and supracardiac shadow 3.2 cm. wide. A roentgenogram of the long bones showed typical periosteal markings of congenital syphilitic bone involvement.

*Comment.*—The positive Wassermann reaction, the roentgen-ray report of the bone changes, the improvement with treatment and no recurrence of symptoms suggest syphilitic bone and joint trouble, with perhaps syphilitic cardiovascular involvement, but it is possible that acute polyarticular rheumatism occurred as a complication of congenital syphilis. The slight cardiac enlargement may have been due to either the rheumatic or the syphilitic involvement; the former seems the more likely. Clinical or roentgen-ray evidence of aortic disease was not present.

Veeder and Jeans [24] reported their case 4,072, which is similar to our cases 1 and 2. They stated that joints are involved in 10 per cent of hereditary syphilitic cases. O'Reilly, in Abt's volume 5, stated that pain is present in joint syphilis, with redness and limitation of motion less frequent.

If in children an aortic regurgitant murmur is heard, the underlying cause should be regarded as rheumatic and inquiry should be made into the previous history as to pains in the muscles, and as to chorea. Veeder and Jeans,[24] in a series of seventy-four patients with congenital syphilis,

found cases of chorea, torticollis, pain in the joints and obscure pains in the muscles, clinical conditions which are usually considered rheumatic; these accounted for 20 per cent of his series. One can readily see from this that aortic or other heart trouble, with such a history, might be called rheumatic when in reality congenital syphilis could be the cause. However, the proof of the syphilitic etiology of the heart disease in any given case is necessary before the more common and so more likely rheumatic factor can be excluded.

CASE 3.—W. G., a man, aged 43, had been treated when young for congenital syphilis. He had teeth of Hutchinsonian type. He complained now of pain over the heart and of shortness of breath. The Wassermann reaction was positive. Examination revealed signs of aortic regurgitation and an aneurysm of the ascending aorta. Roentgen-ray and fluoroscopic examination revealed a pulsating shadow of large size in the heart region. The diagnosis was aneurysm of the aorta.

*Comment.*—It is possible that this man's aortic regurgitation and aneurysm were the result of the congenital syphilis, but at this age one cannot draw definite conclusions. It seems at least as likely that the patient had never had congenital syphilis, but had acquired syphilis some twenty years before.

## SUMMARY AND CONCLUSIONS

1. A review of the literature indicates that the heart and blood vessels may be affected to a considerable degree in congenital syphilis.

2. Of thirty-five cases of congenital syphilis in which autopsy was performed at the Massachusetts General Hospital and Infants' and Childrens' Hospitals in Boston, fourteen (40 per cent) showed *Spirochaetae pallidae* (seven cases) or pathologic changes in the heart or blood vessels (thirteen cases) probably due to syphilis; six cases showed both spirochetes and pathologic changes.

3. Of twenty-five cases of congenital syphilis studied clinically, none showed proof by physical examination or the roentgen ray (done in eight) of syphilitic involvement of the heart or aorta. Several showed signs suggesting cardiac or possible aortic disease, but the likelihood of complicating acute rheumatic infection had to be borne in mind to explain some of the characteristics, as well as symptoms and signs of occasional arthritis. The autopsy results noted here and reported in the literature prove that the heart and aorta may, however, be diseased in congenital syphilis, and so in the examination of children with cardiovascular disease this possibility should always be borne in mind. The wealth of the material in some parts of the world where congenital syphilis is more common than in New England may afford better clinical examples of congenital syphilitic involvement of the heart and

aorta than we were able to find in our small series.[49] It does appear, however, from our study, that well marked clinical evidence of such involvement is not common.

4. Fortunately, in infants with congenital syphilis, the skin lesions and the snuffles direct one's attention to the syphilitic infection at the time when treatment is most efficacious. The involvement of the cardiovascular system under these circumstances may be present but difficult to diagnose.

---

49. Dr. Hugh McCulloch of St. Louis, in a personal communication to the authors, writes that he is to publish shortly an article concerning the rôle played by congenital syphilis in causing heart disease in later life. A question from his letter follows:

"In our Children's Hospital Clinic we have observed in the past 12 years about 1,500 cases of congenital syphilis. Of this number there have been 7 infants who died shortly after birth and at autopsy spirochetes could be demonstrated in the heart muscle as well as in the other vital structures of the body. There were also changes in the heart muscle indicative of a myocardial lesion. These infants all died without symptoms of heart disease and, in my opinion, have died as a result of the fulminating syphilitic infection. In addition there have been four children over two years of age, all white, who had congenital syphilis and during their admission to the hospital were found to have heart disease. In each instance it was easy to recognize that these children were suffering from the rheumatic type of cardiac disease and had no signs of syphilitic heart disease. These children have been followed over a period of several years and it still seems clear that syphilis has had no influence on the heart disease.

"As a result of these observations, we feel very strongly that children who have congenital syphilis and who live to be a year or more of age do not suffer from heart disease, any more than any other normal group of children. Each syphilitic child receives, from time to time, a very careful physical examination, so that we are inclined to believe that we have not overlooked any heart disease in these children."

Drs. James S. McLester of Birmingham, Ala., and George R. Herrmann of New Orleans, in personal communications to the authors, have also expressed their beliefs that congenital syphilis plays little part in the production of cardiovascular disease. Dr. McLester states that this seems to be true even among negroes.

# MICROPRECIPITATION TEST FOR SYPHILIS *

M. G. PETERMAN, M.D.
MILWAUKEE

Originality is not claimed in proposing a microprecipitation test of blood serum and spinal fluid for syphilis. The Kahn [1] test is a modification of the Sachs-Georgi reaction,[2] an extract prepared according to the method of Neymann and Gager [3] and a short period of incubation being used. The basis of most of the precipitation reactions in syphilis is Michaelis'[4] observation that diluted alcoholic extract of a syphilitic liver added to heated syphilitic serum produces a precipitation. A review of the literature may be found in Kahn's book [1] and in an article by Kline and Young.[5]

The time-consuming complexity, the difficulty in standardization and the possible sources of error in the complement fixation blood test have stimulated a search for a more reliable and a simpler test. The Wassermann test is an indirect, empiric procedure requiring five different animal reagents for its completion: human serum (antibody), guinea-pig serum (complement), rabbit serum (amboceptor), sheep red cells and beef heart (antigen). The precipitation tests, of which Kahn's recent modification is the most satisfactory, require only human serum and antigen. The tests have a scientific basis and may be used quantitatively as a chemical reaction.

In pediatric practice it is often difficult to obtain more than small amounts of blood. Kahn proposed a microprecipitation test requiring only 0.025 cc., or one half of a drop of serum.[6] Kline and Young have proposed a micro-Kahn test which is also comparatively simple.[5]

The following microprecipitation test is offered because of its simplicity. It may be carried out in the physician's office in less than twenty minutes. The equipment necessary consists of a pipet graduated in 0.001 cc., a hanging drop slide, a glass slide and a thermometer. (The antigen is prepared according to the method of Neymann and Gager.[3] Beef heart is minced, extracted several times with ether and

* Received for publication March 14, 1927.
* From the Milwaukee Children's Hospital.
* Read before the Chicago Pediatric Society, March 15, 1927.

1. Kahn, R. L.: Serum Diagnosis of Syphilis by Precipitation, Baltimore, Williams & Wilkins Company, 1925.
2. Sachs and Georgi: Med. Klin. **33**:805, 1918; ibid. München. med. Wchnschr. **67**:66, 1920.
3. Neymann and Gager: J. Immunol. **2**:573, 1917.
4. Michaelis: Berl. klin. Wchnschr. **44**:1477, 1907.
5. Kline, B. S., and Young, A. M.: Microscopic Slide Precipitation Test for Syphilis, J. A. M. A. **86**:928 (March 27) 1926.
6. Kahn, R. L.: Micro-Kahn Reactions, J. A. M. A. **87**:2092 (Dec. 18) 1926.

then with alcohol. Cholesterol is added to the final extract. The antigen solution is diluted with physiologic sodium chloride and is ready for use. This antigen may be purchased from the Michigan State Board of Health Laboratories ready for use.) After the serum is inactivated at 56 C. for one-half hour, 0.05 or 0.025 cc. is placed in the concavity of a hanging drop slide; 0.010 or 0.0050 cc. of diluted antigen is added and stirred thoroughly. (For spinal fluid a higher dilution of antigen is used.) The slide is covered with a glass slide and placed in an incubator at 37 C. for ten minutes. (Incubation produces sharper reactions.) The slide is rotated to mix the solution thoroughly and then read, preferably under a microscope; the results are interpreted according to the degree of precipitation, plus one, two, three and four.

Five hundred microprecipitation tests have been made at the Milwaukee Children's Hospital on serums and spinal fluids, with a Wassermann (Noguchi modification) control on all. The serums and spinal fluid were obtained from infants and children ranging in age from prematurity to 15 years. (Several specimens were obtained from parents of the children.) Many of the patients had fever, acute infectious diseases, rachitis and other diseases. A detailed list of diagnoses would be of no particular value. It is sufficient to point out that the microprecipitation test was not influenced by these complications. As will be seen in the tables, a number of the patients had congenital syphilis. The influence of antisyphilitic treatment on the microprecipitation and Wassermann tests will be the subject of another paper. The Wassermann reaction (Noguchi modification) is the first to disappear after treatment, and the last to reappear when treatment is stopped. In 500 tests there was agreement in 455, or 91 per cent. There were only three positive Wassermann tests with negative precipitations. (One of these was repeated and gave negative Wassermann and precipitation tests, as shown in table 3.) There were forty-two positive precipitations with negative Wassermann tests (tables 1 and 2). Both tests were negative in 395 cases; both tests were positive in sixty, and there was disagreement in forty-five.

In the forty-two positive precipitation tests with negative Wassermann reactions, there were seventeen one plus, fourteen two plus, eight three plus and three four plus reactions. Syphilis was demonstrated in all of these cases except two (one patient was a donor for transfusion); eleven patients had had previous three or four plus Wassermann tests and had undergone treatment; twenty-two patients had congenital syphilis, and nine were the parents of children with congenital syphilis.

There were three serums with one plus positive Wassermann reactions and negative precipitation tests. One of the one plus tests was repeated and found negative in both tests; on repetition another revealed a four-plus precipitation test with a negative Wassermann reaction.

TABLE 1.—*One Plus Positive Microprecipitation Tests with Negative Wassermann Reactions*

| Case No. | Precipitation Test | Control Wassermann Test | Previous Wassermann Test | Repeated Precipitation Test | Repeated Wassermann Test | Remarks |
|---|---|---|---|---|---|---|
| 1 | + | — | ++++ | ..... | ..... | Congenital syphilis under treatment |
| 2 | + | — | ..... | ..... | ..... | Donor (lost from observation) |
| 3 | + | — | ++++ | ..... | ..... | Congenital syphilis under treatment |
| 4 | + | — | +++ | ++++ | ++++ | Congenital syphilis under treatment |
| 5 | + | — | ++++ | ..... | ..... | Congenital syphilis under treatment |
| 6 | + | — | ..... | ..... | ..... | Congenital syphilis under treatment |
| 7 | + | — | ++++ | ..... Child | ..... Child | Congenital syphilis |
| 8 | + | — | ..... | ++++ | ++++ | Syphilis |
| 9 | + | — | ..... | ..... | ..... | Congenital syphilis? |
| 10 | + | — | ..... | ..... | ..... | Congenital syphilis |
| 11 | + | — | ..... | ..... | ..... | Syphilitic father |
| 12 | + | — | ..... | ++++ | — | Congenital syphilis |
| 13 | + | — | ..... | ..... | ..... | Syphilitic father |
| 14 | + | — | ..... | ..... | ..... | Mother had several stillbirths and miscarriages |
| 15 | + | — | ..... | ..... | ..... | Congenital syphilis |
| 16 | + | — | ..... | ..... | ..... | Syphilis? |
| 17 | + | — | ..... | ..... | ..... | |

TABLE 2.—*Two, Three and Four Plus Microprecipitation Tests with Negative Wassermann Reactions*

| Case No. | Precipitation Test | Control Wassermann Test | Previous Wassermann Test | Repeated Precipitation Test | Repeated Wassermann Test | Remarks |
|---|---|---|---|---|---|---|
| 1 | +++ | — | ++++ | ..... | ..... | Congenital syphilis under treatment |
| 2 | +++ | — | +++ | ..... | ..... | Congenital syphilis under treatment |
| 3 | +++ | — | ..... | ..... | ..... | Brother four plus Wassermann test |
| 4 | +++ | — | ..... | ..... | ..... | First two pregnancies miscarried |
| 5 | ++ | — | ..... | ++ | ++++ | Congenital syphilis |
| 6 | ++ | — | ..... | ..... | ..... | Congenital syphilis |
| 7 | ++++ | — | ..... | ..... | ..... | Congenital syphilis |
| 8 | ++ | — | ++++ | Child | Child | Syphilis |
| 9 | ++ | — | ..... | ++++ Child | ++++ Child | Syphilis |
| 10 | ++ | — | ..... | ++++ | ++++ | Syphilis |
| 11 | ++ | — | +++ | ..... | ..... | Congenital syphilis under treatment |
| 12 | ++ | — | +++ | ..... | ..... | Congenital syphilis under treatment |
| 13 | +++ | — | ..... | ..... | ..... | Syphilis |
| 14 | ++ | — | ..... | ..... | ..... | Convulsions |
| 15 | ++ | — | ++++ | ..... | ..... | Congenital syphilis |
| 16 | ++++ | — | ..... | ..... | ..... | Congenital syphilis |
| 17 | ++ | — | ..... | ..... | ..... | |
| 18 | ++ | — | — | ..... | ..... | Syphilitic father |
| 19 | +++ | — | — | ..... | ..... | Children had congenital syphilis |
| 20 | ++ | — | ..... | ..... | ..... | Congenital syphilis |
| 21 | ++ | — | ..... | ..... | ..... | Congenital heart disease |
| 22 | +++ | — | ..... | ..... | ..... | Congenital syphilis |
| 23 | ++++ | — | ..... | ..... | ..... | Congenital syphilis |
| 24 | +++ | — | — | ..... | ..... | Congenital syphilis |
| 25 | ++ | — | ..... | ..... | ..... | Mother of child with congenital syphilis |

Dr. T. L. Squier, chief of the department of preventive medicine of the A. O. Smith Corporation, has used this microprecipitation test to check the Wassermann tests made by the Wisconsin Psychiatric Institute. The serums were all taken from adults. There was agreement in 602 of the 609 serums, or 98.8 per cent. Five hundred and ninety-nine serums were negative with both tests, and three were four plus; there was relative agreement in five more, that is, three plus precipitation test with two plus Wassermann test, etc. There were two negative microprecipitation tests with a four and a three plus Wassermann reaction; both of these patients had had treatment. The results of these tests are not included in my total statistics, since the tests and the controls were not made in the laboratory at the hospital.

TABLE 3.—*Negative Microprecipitation Tests with Positive Wassermann Reactions*

| Case No. | Precipitation Test | Control Wassermann Test | Previous Wassermann Test | Repeated Precipitation Test | Repeated Wassermann Test | Remarks |
|---|---|---|---|---|---|---|
| 1 | — | + | ..... | — | — | No evidence of syphilis |
| 2 | — | + | — | ++++ | — | Mother had several miscarriages |
| 3 | — | + | ..... | ..... | ..... | Lost from observation |

## SUMMARY

A microprecipitation test for syphilis is offered because of its simplicity and accuracy.

In 500 tests, the microprecipitation test was positive in 99.4 per cent of the cases in which syphilis was demonstrated. There were three negative precipitation tests with one plus Wassermann reactions. One of these patients was lost from observation; one probably had congenital syphilis, and in the third, evidence of syphilis was not demonstrated. Subsequent precipitation and Wassermann tests on the third patient were negative. Repeated examination of the patient who probably had congenital syphilis revealed a four plus precipitation test and a negative Wassermann reaction.

The Wassermann reaction was positive in 91.6 per cent of the cases in which syphilis was demonstrated.

Fevers, acute infectious diseases, and other conditions did not influence the microprecipitation test.

167 17th St.

# PREVENTION AND TREATMENT OF THRUSH (OIDIAL STOMATITIS)*

HAROLD K. FABER, M.D.
AND
ESTHER B. CLARK, M.D.
SAN FRANCISCO

Thrush, or oidial stomatitis, has been comparatively neglected in recent medical literature,[1] and its importance, both as a clinical and as an epidemiologic problem, has been too generally minimized. Clinically, it is commonly regarded as an innocuous infection, readily curable or self-limited in duration, whereas it is not uncommonly severe and occasionally fatal; not infrequently it fails to yield even to vigorous treatment, and without treatment it may run a course of many weeks. As a problem of institutional hygiene in the prevention and control of epidemics, particularly in wards for new-born infants, its importance is second only to that of impetigo.

It is generally considered that oidial stomatitis is due to contamination from imperfectly sterilized nursing bottles or nipples, from the introduction of unsterile cleansing solutions into the mouth and from the mother's breasts or from the hands of attendants. It is believed that premature, weak, athreptic infants or those suffering from other infectious diseases are especially predisposed to thrush. While we have no reason to dispute any of these beliefs (all of which are doubtless true), none of them offers a solution to the problem presented by the outbreaks of thrush, sporadic at first and later epidemic, in our own hospital. These outbreaks occurred in spite of unquestionably adequate sterilization of all nipples, bottles and solutions entering the infants' mouths and of all clothes and bed linen; in spite of meticulous cleanliness in handling the babies; in spite of rigid avoidance of washing or otherwise touching the inside of the babies' mouths; in spite of careful washing of the mothers' breasts before nursing (although this is admittedly an inadequate procedure) and expressing and discarding the first few drops of milk. It occurred in babies exclusively breast fed, in those almost entirely bottle fed and in those partly breast and partly bottle fed. As a rule, premature infants were spared. Nearly all of the babies in the hospital were healthy and vigorous—

* Received for publication, May 25, 1927.
* From the Division of Pediatrics, Stanford University School of Medicine.
* Read at the meeting of the American Pediatric Society, May, 1927.

1. The last comprehensive review is that of Fischl, R.: Entwicklung und gegenwärtiger Stand unserer Kenntnisse über die Soorkrankheit, Ergebn. d. inn. Med. u. Kinderh. **16**:107, 1919.

some of them exceptionally so. Infections occurred almost exclusively (as will be further detailed) in the babies of the well-to-do private patients; there were few in the babies of the poorer, presumptively less cleanly, clinic patients.

On Jan. 23, 1927, a small epidemic of thrush began which affected eleven babies in all, or 31 per cent of all those born in the private service between January 11 and March 3; the last case began on February 28. Clinically the infections were rather resistant to treatment, but serious complications or sequelae did not occur. In the majority of instances the lesions were detected early and did not become extensive, but there was a striking tendency to recurrence. This epidemic forms the basis of the present report.

It was our task to detect and to eradicate the source or sources of infection. In the hospital there are two nurseries, one for clinic and the other for private patients. The clinic nursery is in the older part of the building; it is small and frequently overcrowded. The private nursery is in the newer part of the building; it is more spacious and rarely overcrowded. Both nurseries open on the same corridor, being separated by a distance of only about 25 feet, and are supplied from the same sources. Each has its separate staff of pupil nurses, but occasionally at night nurses from one ward relieve those in the other. The nurses receive the same preliminary training and employ the same technic. A strict rule has been in force for more than a year that no person other than the nurses assigned to this duty and the porter who scrubs the floors and walls may be admitted to the private nursery. The rule has not been so strictly enforced for the clinic ward, to which the interns and attending physician are also admitted.

All bed linen, baby clothing, gauze and cotton are sterilized in the autoclave and afterward handled with aseptic precautions. All nipples, bottles and soap solutions (Castile) are boiled for twenty minutes. All sugar solutions, formulas and water for feeding are boiled for five minutes. Nurses are required to wash their hands in green soap and water, followed by a rinsing in water and drying on a sterile towel before each handling of the babies. Mothers' breasts are cleansed with soap and water, followed by a rinsing with sterile water. The first drops of milk were expressed and discarded in one series of private cases. For about two years, washing of the mouths of babies has not been permitted. Previously, solutions of boric acid and later sterile water had been used for this purpose, and had been ineffective in preventing thrush.

Faced by a progressing epidemic, we considered chiefly the following possible sources:

1. Faulty sterilization of formulas, sugar solutions, water, bottles and nipples. The rubber nipples were particularly considered.

2. Traumatization of mouths from rubber nipples.
3. Defects in the cleansing of the hands of nurses or other errors of aseptic technic of isolation.
4. Contamination of mouths from mothers' breasts.
5. Hitherto unsuspected resistance of *Oidium* to heat.
6. Defective cleansing of the nurseries.

A check-up of the actual performance of sterilization by boiling showed it to have been systematic and thorough. One may perhaps refer properly to the manifest anxiety of the entire personnel to do everything possible to end the epidemic. Special attention was given to nipples, and after the first few cases of thrush, all the old stock was discarded. The new nipples were thereafter sterilized by autoclaving. Despite this precaution, new cases occurred.

The thermal death point of *Oidium albicans* is said by Plaut [2] to be 60 C. We wished, however, to repeat the experiment on our own cultures and with the mycelial form which is assumed by *Oidium* when

TABLE 1.—*Thermal Death Point of Cultures Containing Large Numbers of Mycelia*

| Temperature Centigrade | Growth |
|---|---|
| 26 (Control) | +++ |
| 51 | ++ |
| 60- 61* | + |
| 68- 73 | 0 |
| 79- 80 | 0 |
| 85- 89 | 0 |
| 98-100 | 0 |

* Note survival at 60, the thermal death point as given by Plaut.

grown under relatively unfavorable conditions, and hence presumptively more resistant to destruction.[3]

For our experiment we used platinum loops dipped in culture, then dipped in sterile water at a given temperature for one minute and stroked on carrot agar slants. The results of the experiment are given in table 1.

Since heating for one minute at from 68 to 73 C. kills mycelia, we have no reason to believe that the five minute boiling period could have been ineffective.

Traumatization of mouths by the slightly rough surface of rubber nipples was thought to have been a possible predisposing cause. For

2. Plaut, H. C.: Die Hyphenpilze oder Eumyceten, in Kolle and Wassermann: Handbuch der Pathogenen Mikroorganismen, ed. 2, 1913, vol. 5, p. 1.

3. The so-called spores or conidia of *Oidium albicans* are unlike the spores of bacteria in size and resistance to heat. *Oidium* also generates survival forms known as chlamydospores, cells several times larger than the yeast forms, filled with reserve food material and adapted to survival without multiplication over long periods of time, but apparently not adapted to resisting great heat.

a time all feedings of formula or water were given by spoon or pipet, but without apparent effect.

Nurses were rigidly questioned and strongly cautioned as to the washing of hands and the enforcement of aseptic isolation precautions within the nursery, and there was little doubt that, within reasonable limits, nursing precautions were being fully observed.

Contamination from the mother's breasts, a possible cause of sporadic cases, could hardly be the source of an epidemic. This possibility was practically ruled out by the character of the epidemic itself, since many of the mothers occupied private rooms and were practically isolated one from another. Special precautions were instituted to safeguard the cleansing of the breasts before nursing, but without apparent effect.

The nurses on duty did not report any defects in the cleaning of the nurseries. The cribs, stands, bathing and washing tables and scales were cleaned by the nurses themselves. The floors were cleaned daily and the walls twice a week by a porter. No other persons were admitted to the private nursery. This rule had been laid down some years before and was considered necessary to avoid the overcrowding and multiplication of contacts incidental to a multiplicity of attending physicians and special nurses.

The first survey, then, appeared to show that none of the causes described was operative. As the epidemic progressed, however, one striking fact became manifest; namely, that with a single exception all the cases were occurring in the private nursery. Only one case occurred in the clinic nursery, in spite of the somewhat less rigid technic and the somewhat greater likelihood of maternal contamination. This fact, once established, served to rule out definitely several possible sources of infection; namely, bottles, nipples, formulas, water, clothes and dressings; defective sterilization; maternal infection from breasts, and oral traumatization. All these factors were common to both nurseries. It ruled out the probability, though not the possibility, of defective technic in nursing. It pointed strongly in the direction of a local cause in the private nursery itself. A more careful inspection was made. The floors, beds, dressing table, washing table, closet shelves and scales were clean. There was a little dust on the window sills, but no more than might accumulate within a few hours; but in the angle over the washing table formed by the galvanized water tank and the wall, behind the pipes which ran close to the wall and down to the table and in the screen covering the pipe exit under the table were heavy accumulations of dust. These were places unusually difficult to reach in cleaning, and they could not be seen readily. The tank and pipes were set close to the wall. In the clinic nursery such accumulations were not found. Here the tank and pipes were set out 1 or

2 inches (2.54 or 5.08 cm.) from the wall, and the exit for pipes under the washing table was closed by a smooth metal plate.

Removal of the dust deposits was immediately followed by a cessation of the epidemic. Further cases have not occurred in the two months that have since elapsed. Direct smears from the dust showed mycelial threads. The cultures unfortunately were overgrown by other organisms, chiefly a yeast-like organism (not *Oidium*) developing ascospores, fungi of the *Aspergillus* group and various bacteria, including "spreaders."

Incidental to this study we have had occasion to test certain therapeutic materials, particularly boric acid, alkalis, formaldehyde and two dyes, mercurochrome-220 soluble and gentian violet, and we take this occasion to report on them briefly.

In spite of the long recognized worthlessness of boric acid as an antiseptic, this substance continues to be recommended in most textbooks on pediatrics and to be used by many practitioners for the

TABLE 2.—*Results Showing Effect of Boric Acid on Growth of Oidium Albicans*

| Concentration Boric Acid, per Cent | In Original | In Agar Transplant at 48 Hours |
|---|---|---|
| Control | ++ | ++ |
| 1 | + | ++ |
| 2 | + | ++ |
| 3 | + | ++ |
| 4 | + | ++ |
| 5* | + | + |

* Saturated solution.

prevention and treatment of infections of the mouth and eye. Our experiments, though not new, were repeated for confirmation. We used carrot infusion. In all original tubes *Oidium* multiplied slowly but grew abundantly on transplants. *Oidium* kept in 5 per cent boric acid in carrot infusion for six days multiplied abundantly on transplant agar. The experiments show clearly that boric acid even in saturated solution does nothing more than inhibit multiplication of *Oidium albicans,* and that the organism readily survives exposure to such solutions for considerable periods of time.

Because of the frequent use of alkaline solutions in the local treatment of patients with thrush, cultures were grown at varying degrees of hydrogen ion concentration. Carrot infusion was used. Growth was equal in all tubes, and there were no differences in the character of growth in regard to yeast forms and mycelia. The results are shown in table 3.

The experiment shows that *Oidium albicans* is adapted to growth in a wide range of hydrogen ion concentration, multiplying freely at the highly alkaline point of $p_H$ 10, which is greater than could be maintained in the mouth for more than a brief time.

A few experiments made by one of us (C.) showed that half a minute after swabbing infants' mouths with 2 per cent sodium bicarbonate solution, the reaction in the mouth was from $p_H$ 8.4 to $p_H$ 8.8. The reaction returned to normal in from one-half to one and one-half hours. The average reaction of the untreated mouth was from 4.4 to 6.

Formaldehyde is frequently used in the treatment of patients with thrush, usually in 1 per cent solution of formaldehyde (0.4 per cent formaldehyde). The results in table 4 show the effect of varying concentrations of this antiseptic on *Oidium albicans.*

The experiments show that the effective strength of formaldehyde is between 1 : 500 and 1 : 2,000. The rather feeble penetrating powers of the substance and its rapid dilution by the secretions of the mouth,

TABLE 3.—*Results Showing Effect of Varying H Ion Concentration in Growth of Oidium Albicans*

| $p_H$ | | | $p_H$ | | |
|---|---|---|---|---|---|
| 4* | 5* | 6.6† | 8‡ | 9‡ | 10‡ |
| ++ | ++ | ++ | ++ | ++ | ++ |

* Hydrochloric acid added.
† Reaction of medium.
‡ Sodium hydroxide added.

TABLE 4.—*Effect of Liquor Formaldehyde on Growth of Oidium Albicans*

| Solution of Formaldehyde | Formaldehyde | Growth | |
|---|---|---|---|
| | | Original Carrot Infusion | Transplant to Agar Slant at 24 Hours |
| 1:250 | 1:625 | 0 | 0 |
| 1:500 | 1:1250 | 0 | slight (delayed) |
| 1:1000 | 1:2500 | slight | slight |
| 1:2000 | 1:5000 | moderate | good |
| 1:5000 | 1:12500 | good | good |

especially abundant in the presence of thrush, make it doubtful whether an effective concentration could be maintained long enough to sterilize the areas of infection, even when a solution stronger than 1 per cent solution of formaldehyde is used.

The ideal antiseptic for the treatment of patients with thrush should combine rapid penetration with minimal toxicity. These requirements would appear to be best met by some of the dyes. In 1892, Taube [4] reported good results from the use of pyoktanin (methyl violet) in 10 per cent solution. Usually one application was enough, but there were occasional recurrences. Plaut supported Taube's clinical observations by finding that *Oidium* scraped from the hard palate after treat-

4. Taube: Pyoktanin gegen Diphtherie, Scharlachdiphtherie, Tonsillitis und Soor, Deutsche med. Wchnschr. **18**:862, 1892.

ment would not multiply in vitro. In 1921, Maier [5] successfully treated seven patients who had thrush, three infants and four adults, with acriflavine, noting in the infants that the lesions disappeared in from two to three days when previously no effect had been obtained with boric acid or borax.

In 1925, Faber and Dickey [6] advocated the use of gentian violet in the treatment of patients with thrush. Churchman [7] had already shown that this dye is effective against *Oidium albicans* in high dilutions, and in 1926, Clark [8] made quantitative measurements of its inhibiting and lethal effects. In table 5, reproduced from her report, are given the results of her tests.

Its high bactericidal value, together with its powers of rapid penetration into surface tissues and its negligible toxicity would appear to confirm Faber and Dickey's clinical observations of the value of gentian violet in the treatment of patients with thrush. Mercurochrome-220 soluble is decidedly less effective.

TABLE 5.—*Effect on Oidium Albicans of Varying Dilutions of Gentian Violet in Carrot-Infusion Agar*

| Dilution of Gentian Violet | Growth |
|---|---|
| 1:100 | 0 |
| 1:10,000 | 0 |
| 1:25,000 | 0 |
| 1:50,000 | Very slight |
| 1:75,000 | Very slight |
| 1:100,000 | Slight |
| 1:500,000 | Good |

## COMMENT

The prevention of epidemic outbreaks of thrush, especially in hospital wards for small babies should not be a difficult matter, providing the known safeguards are meticulously observed. In our opinion, based on our own experience and a consideration of the experiences of others, thrush is probably due to gross contamination. In theory, such contaminations should never occur in modern well managed hospitals. In practice they may do so, through oversight or undetected neglect of precautions which are assumed to have been carried out.

The sources of infection which we consider to be of the greatest importance are: (1) the oral secretions and stools of patients with

5. Maier, M.: Ueber Trypaflavinwirkung bei Erkrankungen der Mund-und Rachenhöhle, besonders bei Soor, München. med. Wchnschr. **68**:1586, 1921.

6. Faber, H. K., and Dickey, L. B.: The Treatment of Thrush with Gentian Violet, J. A. M. A. **86**:900 (Sept. 19) 1925.

7. Churchman, J. W.: The Selective Bacteriostatic Action of Gentian Violet and Other Dyes, J. Urol. **11**:1, 1924.

8. Clark, E. B.: Effect of Gentian Violet and Mercurochrome on Endomyces Albicans, J. Infect. Dis. **40**:423 (March) 1927.

thrush and (2) dust. The most important routes of transmission are: (1) hands, (2) bottles and nipples and (3) air currents. The precautions which we consider necessary to avoid infection are as follows:

1. Scrupulous cleanliness in the nursery, maternity ward or mother's room, and formula kitchen. Accumulations of dust in walls, sills, moldings, pipes, tanks and shelves, must be rigidly prevented. Complete cleaning not less often than twice a week is necessary. Cleaning must be done in such a way that dust is prevented, as far as possible, from circulating through the air.

2. Adequate sterilization of bottles and nipples. Boiling for five minutes or even less is sufficient.

3. Cleaning of the hands of nurses or other attendants with soap and water before handling each baby, and after changing diapers, especially those containing stool.

4. No washing of babies' mouths.

5. Inspection of babies' mouths at least once daily for evidence of thrush, and immediate isolation of suspected cases.

We consider these precautions as the most important. None of them is new. It is our purpose merely to emphasize the absolute necessity of having them all carried out thoroughly and constantly. Frequent inspection by the supervising personnel is essential.

We wish to add a word of protest against the use of boric acid solutions, still a common practice, for the purposes of cleansing babies' mouths and eyes and the mothers' breasts. We are confident not only that this procedure is without value, but also that it may at times be responsible for the propagation of infection. The sense of security which its use seems to give is wholly without foundation, and has doubtless led to the neglect of useful precautions.

It might be well to call attention to the occasional occurrence of oidial infections in adults as a possible source of thrush in infants. Almost any of the mucous membranes may be affected, vaginal infection being not uncommon. We recently saw a case of thrush in an infant whose mother had had vaginal thrush prepartum. The nipples may occasionally be infected with *Oidium,* but this is probably rare except when the primary source is the baby's mouth. It is highly desirable that the obstetrician watch for signs of thrush in the mother, and, finding them, advise isolation of her baby.

The treatment of a patient who has thrush may follow one of two lines: simple cleansing or the use of antiseptics. For the first, alkaline, but not too alkaline, solutions frequently applied to the mouth may result in cure after a week or two, especially in healthy infants and in infants with mildly virulent strains of *Oidium.* The outcome of such treatment is, however, always problematic, and against relatively virulent strains such as we have often seen, is practically certain to be disappointing. Boric acid is not only valueless, but, as the recent experience in Chicago demonstrated, dangerous. We emphasize the point

because a recent text in a book on pediatrics recommends the Escherich boric acid sac or teat. This is a small sac of silk or batiste filled with boric acid powder sweetened with saccharin which is placed and left in the infant's mouth, presumably until the thrush is cured. It is possible that boric acid poisoning might result from such treatment. Solution of liquor formaldehydi has never given us satisfactory results, and we believe that the reason is its poor penetration and its rapid dilution by the secretions of the mouth below the point of disinfecting efficiency. With mercurochrome-220 soluble we have obtained occasional but not constant retrogression of the oral lesions. With gentian violet we have obtained better and more constant results than with any other substance. To obtain them, however, it is necessary to follow certain rules. Treatment should be given at least one hour after feeding. The mouth should be gently cleansed with several cotton swabs to remove the adherent mucus over the affected areas—a most important precaution, since as Churchman[9] has shown, the dye is absorbed and its therapeutic effect on the lesion annulled by overlying secretion. The dye, in 1 per cent aqueous solution, must be freshly prepared (not more than a few days old) and must be applied generously, first to the affected area and then over the tongue and in the buccogingival folds. The treatment must be repeated once or twice daily for at least three successive days, and, if possible, every other day thereafter for from one to two weeks. The mother's breasts should be carefully cleansed with soap and water before each nursing, and the first few drops of milk discarded to prevent reinfection.

If this technic is followed, the lesions will have nearly disappeared by the second day and entirely so by the third; new ones will not appear. If only one or two treatments are given, recurrences will frequently occur, usually in other areas than the site of the original lesion. In spite of the deep staining of the entire oral cavity, which persists for a day or two after treatment has been stopped, there is no apparent interference with the baby's appetite or ability to feed. Stain on the lips or chin can be easily removed with a little alcohol. The stools during treatment often appear purplish.

SUMMARY

An epidemic of thrush in new-born infants is described, which developed and spread in spite of apparently active and adequate precautions. The source was traced to accumulations of dust in places difficult of access and invisible to casual inspection. Removal of these accumulations was immediately followed by cessation of the epidemic.

---

9. Churchman, J. W.: The Anilin Dyes in Therapeutics, J. A. M. A. **79:** 1657 (Nov. 11) 1922.

*Oidium albicans* succumbs readily to brief exposure to moist heat well below the boiling point. Its growth is barely inhibited by boric acid, in saturated solutions of which it survives for considerable periods (over a week). It grows freely in both an acid and an alkaline medium within the wide range of from $p_H$ 4 to $p_H$ 10. It is killed by 1:250 solution of formaldehyde but not by 1:500. It is destroyed by gentian violet in 1:25,000 solution. Treatment with gentian violet is recommended as the most effective when carried out as described. Boric acid is without antiseptic value and may be dangerous.

# ETIOLOGY OF RESPIRATORY DISEASE IN THE CITY AND COUNTRY SCHOOL OF NEW YORK CITY*

EDITH M. LINCOLN, M.D.
NEW YORK

A recent report outlined the health program at the City and Country School and showed the importance of the respiratory diseases as a cause of absence. The following study was undertaken to analyze the factors that might conceivably influence the frequency of respiratory infections in schools.

During the school year 1923-1924, the school had an enrolment of 132 children, aged from 3 to 12 years. Every child was examined by the school physician, and an analysis was made of the stool and urine. In many cases roentgenograms of the chest were made. The mother of each child handed in a diet list for forty-eight hours, which was checked and discussed at the time of the examination. Information about health habits was obtained at this time from the medical and physical histories compiled by the registrar, who also filled out a special questionnaire regarding conditions in the home. A great deal of this material was checked by the physician through interviews with the mother and from other sources of information. In some cases a second, measured diet list for one or two days was requested.

During the school years 1921-1922, 1922-1923 and 1923-1924, the following measures were taken for the prevention of respiratory diseases: Children with fresh colds were excluded from school for three days, or until the state of acute infection as evidenced by profuse nasal discharge was passed. All children returning to school after an absence for any cause had to be examined by the school nurse before they could return to their classrooms. The teachers were supposed to report promptly any fresh cold noticed in the classrooms. Since the nurse kept the record of attendance by going to the classrooms each morning, she was able to see every child daily; consequently, few children with fresh colds escaped notice. The nurse also supervised the ventilation of the rooms and made a daily round of the yards and roofs to determine when outside play might be permitted. She also decided what outdoor clothes should be worn. All children were supposed to have sweaters as well as coats at school, and dry clothing, especially stockings, was kept on hand by the nurse. Because the younger groups have always had more colds than the older groups, and in order to protect them as far as possible from acute contagious

*Received for publication, April 19, 1927.
*From the Bureau of Educational Experiments, New York.

diseases, every attempt was made to keep them separated from the older children. They had their outdoor play space on the roof and did not go to any special classrooms. The groups, aged 3 and 4, had only a morning session. The 5 year olds remained for the full school day, but they had their lunch and rest apart from the rest of the school.

In spite of these preventive measures, the rate of absence due to respiratory diseases, which include common colds, tonsillitis, grip, influenza, etc., was not markedly reduced. This, also, has been the experience of other school physicians who have made similar attempts to reduce the morbidity from colds.[1] In tabulating these records, cases of pneumonia have not been included among the respiratory infections, because of the prolonged absences which invariably follow these illnesses. After the other respiratory infections, a child returns to school after a brief convalescent period, but almost invariably after pneumonia the child is kept out of school long after his ordinary convalescent period. Consequently, a false idea of the record of absences is created. In the records of these three years, only six cases of pneumonia have occurred. Chart 1 shows the slight but steady decline in the total rate of absences due to illness as compared to the variability and slight decline in the rate of absences due to respiratory diseases.

An analysis of the record of absences in the classes is shown in chart 2, which gives the percentage of absences due to respiratory disease in each group.

It will be seen that, on the whole, age is a determining factor in the percentage of respiratory infections. That this is not the only determining factor, however, is shown by the record of group III in 1921-1922, which had the second best record in the school. A second determining factor is apparently seasonal, as brought out in Townsend's recent report.[2] He studied groups of students in widely separated parts of the United States and reports that "the synchronous variations of the incidence of respiratory affections in the localities as widely scattered as San Francisco, New Orleans, Chicago, Boston and Washington is unmistakably shown and is of extreme interest."

Following the apparent failure of these preventive measures, an intentive study of 1923-1924 was undertaken. A record of weather conditions was kept and studied in relation to the time of the most marked frequency of respiratory disease, but no correlation could be made. There were, of course, more colds in winter, and the more adverse weather conditions occurred during the same general period. On the other hand, a study of the weather report day by day in connection with the record of attendance

1. Mason, H. H.: Some Records Regarding Absences and Their Causes in Lincoln School of Teachers' College, Am. J. Dis. Child. **22**:507 (Nov.) 1921.
2. Townsend, J. G.: Pub. Health Rep. **39**:2669 (Oct. 24) 1924.

does not show that the more frequent colds followed unusually wet or changeable weather. Naturally, this year, as in the past, an occasional outbreak of respiratory disease may have followed a chilling due, for example, to poor judgment in allowing the children to play out of doors when the ground was too wet, or a group of cases of grip may have followed a single case, but on the whole the individual factor

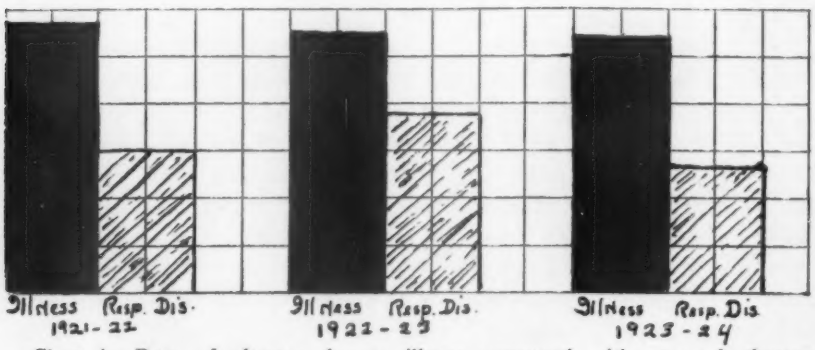



Chart 1.—Rate of absence due to illness compared with rate of absence due to respiratory disease. One square equals 2 per cent.

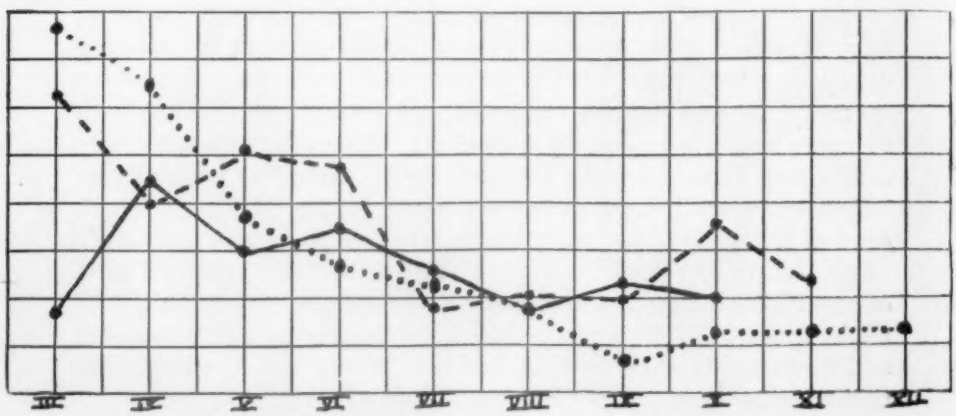



Chart 2.—Percentage of absences in each group due to respiratory diseases. The solid line indicates the years 1921-1922; the broken line, 1922-1923, and the dotted line, 1923-1924. One square equals 2 per cent.

seemed to be dominant in the resistance to infections of the upper respiratory tract.

In order to find out whether there were any other factors in our school group, which determined the greater occurrence of respiratory infections among the younger groups, a study was made of the school environment of each group, chiefly of the classroom and the teacher. The health of the teachers was uniformly good, none of them having

chronic diseases of the upper respiratory tract. The majority of them were careful about noticing fresh colds and seeing that extra clothing was worn in the corridors, etc. The teachers of groups XI and XII were not as careful in these respects, and perhaps the rising percentage of respiratory disease in these groups might be related to this fact. Several of the classrooms were difficult to ventilate and were apt to get too hot (a temperature of from 65 to 68 Fahrenheit was aimed at), but no analogy can be drawn between these rooms and the rate of colds. It is striking, however, that the two rooms that were constantly reported to the physician's office as "too cold" (groups V and VI *A*) show a marked decline in the rate of morbidity of colds. As no other factor except, possibly, physical conditions was found to explain the number of respiratory diseases in the school nor any factor except age to explain

TABLE 1.—*Relationship Between Enlarged and Infected Tonsils and Other Diseases of the Respiratory Tract*

| | Number of Children | Normal Tonsils or Tonsils Completely Removed* | Infected Tonsils | Percentage of Upper Respiratory Tracts Infected | Diseases of the Respiratory Tract Other Than Infected Tonsils |
|---|---|---|---|---|---|
| Children who lost 0 days owing to respiratory disease..... | 31 | 22 | 9 | 30% | |
| Children who lost more than 0 but under 5 per cent.... | 55 | 38 | 17 | 31% | 1 asthma<br>2 adenoids<br>1 sinusitis |
| Children who lost more than 5 per cent but under 10 per cent ..... | 29 | 22 | 7 | 38% | 1 fibrosis of the lung |
| Children who lost more than 10 per cent but under 20 per cent ..... | 17 | 8 | 9 | 59% | 1 sinusitis |
| Children who lost more than 20 per cent..... | 5 | 2 | 3 | 60% | |

* In this group are included several cases of incomplete removal of the tonsils in which no evidence of infection was found.

its gradual decrease in the older groups, a study of the individual children was undertaken. The results of the physical examination of each child were carefully analyzed, and the condition of the nose and throat seemed to be the only factor that bore any relationship to the frequency of colds.

Table 1 shows the relationship between enlarged and infected tonsils and other diseases of the respiratory tract and the record of absences.

As can be seen in table 2, there is no correlation between the state of nutrition and the amount of respiratory disease.

The home environment of each child was studied, including such points as: the type of home—modern or old house, apartment, etc.; the kind of heating; the exposure of sleeping rooms; the sleeping conditions; the health of the parents, of the other children and of the servants. This study did not bring out any factors which varied with the frequency of respiratory diseases. No relationship could be established between types of heating and the frequency of colds.

For purposes of brevity other normal tables are omitted.

A study of the health habits of each child, including his diet, was then undertaken. No correlation could be established between frequency of colds and kind of clothing, nor did the time of the daily bath or the use of cold showers prove determining factors. The facts regarding constipation were equally inconclusive.

The diet lists were studied, first, to determine the approximate number of calories taken daily. It was impossible to evaluate them at all accurately, but it was evident that the intake varied widely in

TABLE 2.—*The Relation of Nutrition to the Frequency of Respiratory Disease*

| | No. of Children | Normal weight * | Underweight | Overweight | Per Cent Normal Weight |
|---|---|---|---|---|---|
| Children who lost 0 days owing to respiratory disease..... | 31 | 26 | 4 | 1 | 84 |
| Children who lost more than 0 but under 5 per cent.... | 55 | 46 | 7 | 2 | 84 |
| Children who lost more than 5 per cent but under 10 per cent..... | 29 | 20 | 8 | 1 | 70 |
| Children who lost more than 10 per cent but under 20 per cent..... | 17 | 14 | 3 | 0 | 82 |
| Children who lost more than 20 per cent..... | 5 | 5 | 0 | 0 | 100 |

* This group includes all children less than 10 per cent underweight or overweight for height.

TABLE 3.—*The Relation of Types of Heating to the Frequency of Respiratory Disease*

| | No. of Children | Steam | Hot Air | Hot Water | Gas | Coal | Per Cent Steam |
|---|---|---|---|---|---|---|---|
| Children who lost 0 days owing to respiratory disease..... | 31 | 22 | 1 | 0 | 4 | 4 | 71 |
| Children who lost more than 0 but under 5 per cent.... | 55 | 39 | 6 | 2 | 4 | 4 | 71 |
| Children who lost more than 5 per cent but under 10 per cent..... | 29 | 18 | 7 | 0 | 2 | 2 | 63 |
| Children who lost more than 10 per cent but under 20 per cent..... | 17 | 12 | 1 | 0 | 2 | 2 | 75 |
| Children who lost more than 20 per cent..... | 5 | 4 | 1 | 0 | 0 | 0 | 80 |

each group. On the whole, as might be expected, the well nourished children ate more than the thin ones, and the active children more than the quiet ones. But no possible relationship could be established between caloric intake and the occurrence of colds. The diets varied widely in the relative amount of protein, fat and carbohydrate taken, and with the first calculations it became evident that a correlation could be made between the amount of carbohydrate intake and the amount of absence due to respiratory disease. A simple method of ranking the diets was evolved and the grouping of the diets into high carbohydrate, moderate carbohydrate and low carbohydrate was checked by several people with almost 100 per cent agreement. Into the group

of high carbohydrate diet were put all the diets that contained cereal twice a day as well as a mid-day starchy vegetable and those diets in which, besides cereal once daily, starchy desserts were stressed and the main supper dish was starchy, or a large amount of bread or sweets were eaten. Moderate carbohydrate diets gave a cooked cereal for break-

TABLE 4.—*The Relation of Carbohydrate Intake to the Frequency of Respiratory Disease*

| | No. of Children | Low CH | Mod. CH | High CH | Per Cent High CH |
|---|---|---|---|---|---|
| Children who lost 0 days owing to respiratory disease..... | 31 | 9 | 14 | 8 | 26 |
| Children who lost more than 0 but under 5 per cent .... | 55 | 10 | 27 | 18 | 33 |
| Children who lost more than 5 per cent but under 10 per cent..... | 29 | 4 | 13 | 12 | 41 |
| Children who lost more than 10 per cent but under 20 per cent..... | 17 | 1 | 4 | 12 | 71 |
| Children who lost more than 20 per cent..... | 5 | 0 | 0 | 5 | 100 |

TABLE 5.—*The Relation of Carbohydrate Intake to the Frequency of Respiratory Disease in Children More Than Six Years of Age*

| | No. of Children | Low CH | Mod. CH | High CH | Per Cent High CH |
|---|---|---|---|---|---|
| Children who lost 0 days owing to respiratory disease..... | 30 | 8 | 14 | 8 | 26 |
| Children who lost more than 0 but under 5 per cent..... | 46 | 6 | 25 | 15 | 33 |
| Children who lost more than 5 per cent but under 10 per cent..... | 20 | 1 | 10 | 9 | 45 |
| Children who lost more than 10 per cent but under 20 per cent..... | 8 | 0 | 2 | 6 | 75 |
| Children who lost more than 20 per cent..... | 0 | 0 | 0 | 0 | 0 |

TABLE 6.—*The Relation of Carbohydrate Intake to the Frequency of Respiratory Disease in Children Aged Six Years and Under*

| | No. of Children | Low CH | Mod. CH | High CH | Per Cent High CH |
|---|---|---|---|---|---|
| Children who lost 0 days owing to respiratory disease..... | 1 | 1 | 0 | 0 | 0 |
| Children who lost more than 0 but under 5 per cent..... | 9 | 4 | 2 | 3 | 33 |
| Children who lost more than 5 per cent but under 10 per cent..... | 9 | 3 | 3 | 3 | 33 |
| Children who lost more than 10 per cent but under 20 per cent..... | 9 | 1 | 2 | 6 | 67 |
| Children who lost more than 20 per cent..... | 5 | 0 | 0 | 0 | 100 |

fast and either a starchy dessert for dinner or supper, or in a few cases, a large amount of cereal with a small amount of bread and potato and no starchy desserts. In the low carbohydrate diets, the main carbohydrate dishes were a breakfast cereal, a starchy vegetable, such as potatoes, once daily, not more than one whole slice of bread a meal, only occasional puddings and little or no candy.

Table 4 illustrates the tabulation of the cases according to carbohydrate intake in relation to absences due to respiratory disease. The correlation is striking. The point at once arises that younger children always are known to have a greater incidence of respiratory infections and that they eat more carbohydrates, because many are on a diet of cereal twice a day, as still prescribed by some physicians.

In tables 5 and 6, the correlation between the amount of carbohydrate in the diet and the absences from respiratory disease is presented separately for children in the 3, 4, 5 and 6 year old groups and for those in the older groups. It will be seen that the correlation holds as well for the older children as for the younger.

## CONCLUSIONS

1. A statistical study of absence from school due to respiratory diseases is presented.

2. Environmental factors in the classroom and home of each child, were studied, as well as the results of the physical examinations and a careful survey of his diet.

3. The only direct correlations obtained were between absences due to respiratory disease and the presence of abnormal conditions in the upper respiratory tract and between absences due to respiratory disease and the amount of carbohydrate in the daily diet of the child.

# CHVOSTEK'S FACIALIS SIGN IN NEW-BORN INFANTS*

FRANK E. STEVENSON, M.D.

A. GRAEME MITCHELL, M.D.

AND

CARL A. KOCH, M.A.

CINCINNATI

In cases of tetany, Chvostek[1] called attention to sudden, tic like contraction of certain muscles supplied by the facial nerve which was elicited by tapping over the middle of the cheek. Later, similar phenomena such as Schultze's sign, Weiss' sign, Lust's sign, Trousseau's sign and the femoralis reflex have been pointed out as being of diagnostic value in tetany. All of these signs vary in the frequency with which they are found in tetany as well as in their diagnostic value. Probably not one of them can be accepted alone as being unquestionably pathognomonic of tetany. Various theories have been advanced in explanation of the mechanism of these phenomena. It has been thought that the hyperirritability may be localized in the muscle itself, that a spinal reflex is involved, or that there is spasm of the blood vessels of the nerves. The consensus of opinion, however, is that the nerve trunk itself is hypersensitive as a consequence of the lowered amount of calcium present.

Of the signs mentioned, that of Chvostek is the most widely employed. The significance that has been attached to the presence of this sign from time to time is of interest. A number of studies, which it is not necessary to quote, have apparently demonstrated that the presence of a positive facial phenomenon (as Chvostek's sign is often called) in older children is not diagnostic of tetany. In early life, however, there is unanimity of opinion that a positive Chvostek's sign means tetany and tetany only. In the numerous investigations on this point, the conclusion reached has usually been that if Chvostek's sign is found in children under 2 years of age, careful study will always show other unmistakable signs of tetany.

In view of this prevailing opinion, we were interested to find that young infants frequently manifested the facial phenomenon without having either clinical or serologic evidences of tetany. We therefore determined the incidence of the positive Chvostek sign in a group of

* Received for publication, May 25, 1927.

* Read at the Annual Meeting of the American Pediatric Society, Chesapeake Bay, May, 1927.

* From the D. K. Rachford Department of Pediatrics, University of Cincinnati College of Medicine.

1. Chvostek: Wien. med. Presse **19**:821, 1878.

normal, new-born infants. New-born infants were selected because it is generally conceded that tetany is a condition which does not occur until about 5 or 6 months of age. In several instances, we have observed manifestations of spasmophilia in the first few months of life, and this has been the experience of other clinicians. Wolff,[2] Nassau,[3] Powers [4] and Griffith [5] have all reported cases in which infants under 2 months of age had active clinical manifestations of tetany. In most of these cases, the diagnosis was confirmed by electrical hyperirritability or a lowered blood calcium or by both.

Our observations were made on infants ranging in age from 12 hours to 21 days. Each infant was tested not only for Chvostek's sign, but also for Schultze's, Lust's, Weiss' and Trousseau's signs as well as for the femoralis and sucking reflexes. Blood calcium determinations were made on all of them, and on some the electrical reactions were ascertained. The infants were all normal except for icterus neonatorum, which was present in many cases. Infants showing evidence of birth trauma, or having abnormal temperature, gastro-intestinal disturbance, convulsions, dehydration or the like were excluded from this study.

Certain sources of error are associated with the elicitation of Chvostek's sign. The intensity of the reaction varies from day to day; the sign disappears temporarily following a convulsion, and it may diminish or disappear at the onset of fever or in extreme malnutrition. Other errors may arise from faulty technic. Concerning the latter, we may mention here that care must be taken in regard to the nature of the blow, which should be a sharp forceful tap with the finger at a point midway between the corner of the mouth and the angle of the jaw. It should be noted, too, that the sign is not obtained in the crying or struggling infant. We found, for example, that the sign was seldom present even in the quiet infant when awake, but was readily demonstrated in the sleeping one. Again, certain pseudoreactions cause confusion. Thus, a fat wave may be obtained in the well-nourished infant or the sucking reflex may be elicted. The sucking reflex is in reality different from Chvostek's sign, consisting of a more or less deliberate pursing of the lips in a downward and forward direction.

In our examinations, the sign was considered positive when a contraction was obtained at one or more of the following places: the lip, the alae nasi and the forehead. The twitching of the lip was

2. Wolff: Arch. f. Kinderh. **66**:385, 1918.

3. Nassau: Ztschr. f. Kinderh. **28**:310, 1921.

4. Powers, T. F.: Tetany as a Cause of Convulsions in Very Young Infants, J. A. M. A. **84**:1907 (June 20) 1925.

5. Griffith, J. P. C.: Blood Calcium in Spasmophilia, J. A. M. A. **86**:828 (March 20) 1926.

most often obtained, followed in frequency by that of the alae nasi and next by that of the forehead.

## SUMMARY OF RESULTS

A total of fifty-five infants, varying in age from 12 hours to 21 days, was examined. Eighty-four per cent were under 1 week of age, 9 per cent under 2 weeks and 7 per cent under 3 weeks. Fifty-four and five-tenths per cent of the infants were colored and 45.5 per cent were white. All of the infants had a positive Chvostek sign. The intensity of the sign varied, as shown in the accompanying table.

*Variations in Intensity of Chvostek's Sign*

| Contraction of | Number Examined | Per Cent |
|---|---|---|
| Lip only | 19 | 34.5 |
| Lip and nose only | 30 | 54.5 |
| Lip, nose and forehead | 6 | 11.0 |

Blood calcium determinations were made after the method of Clark and Collip.[6] In infants under the age of 1 week, the estimations were made on placental blood and in the older ones on venous blood obtained from the longitudinal sinus. Howland and Marriott [7] found that the normal blood calcium was from 10 to 12 mg. per hundred cubic centimeters of serum irrespective of age and regardless of whether the estimations were made on placental blood or on the patient's venous blood. In our series of infants, the blood calcium was between 10 and 12 mg. in all but five instances. In four infants, the calcium was between 8 and 10 mg. and in only one was it less than 8 (7.3 mg.). Since tetany practically never develops until the blood calcium falls below 8 mg., even these infants can be included in the normal group, or at least it can be said that they were not spasmophilic subjects. The infants whose blood calcium was between 8 and 10 mg. did not have a more intense Chvostek's sign than those with a higher blood calcium. The question naturally arises whether in these infants the calcium, while usually present in normal total amount, might be unutilizable because of lack of ionization. In two infants, the calcium ion in the blood serum was estimated by employing the formula elaborated by Behrendt.[8] According to him, the degree of calcium ionization is proportionate to the concentration of the hydrogen ion, the bicarbonate ion and the phosphate ion. His formula is as follows:

$$Ca'' = \frac{61.98 \cdot H'}{\sqrt{(HCO_3) \cdot HPO_4)}}$$

6. Clark and Collip: J. Biol. Chem. **63**:461, 1925.
7. Howland and Marriott: Quart. J. Med. **11**:289, 1917-1918.
8. Behrendt: Biochem. Ztschr. **146-147**:318, 1924.

In one infant, the ionized calcium was 1.9 mg. per hundred cubic centimeters and in the other 1.5. We are unable to state whether these are normal values because of the differences of opinion in this matter.

Electrical reactions were obtained in fifteen infants, and in all instances these were normal.

Schultze's sign (contraction of the muscles supplied by the facial nerve obtained by gentle stroking of the cheek), Lust's sign (eversion of the foot obtained by tapping the external popliteal nerve as it winds around the head of the fibula) and Trousseau's sign were not elicited in any of the infants. Weiss's sign (a contraction of the orbicularis paipebrarum obtained by tapping 2 cm. outside of the external canthus of the eye) was found positive in six of the fifty-five infants and did not bear any relation to the intensity of Chvostek's sign. The femoralis reflex (a forward kick of the leg obtained by percussing over the anterior surface of the thigh at the junction of the upper and middle thirds) was elicited in thirty-eight infants. This reflex was more likely to be present in those infants with an intense Chvostek sign. The sucking reflex, which has been previously described, is readily distinguished from the facial phenomenon. It was obtained in the majority of the cases, usually, however, only after repeated or distinctly forceful percussion of the cheek. If both the facialis and the sucking reflexes were elicited by the same blow, the former always preceded the latter.

## CONCLUSIONS

1. It was found that Chvostek's sign occurred consistently in normal new-born infants.

2. It was always possible to elicit the sign in sleeping infants but when the patient was awake, even though quiet, the reaction was frequently negative. In crying or restless infants, the sign was never obtained.

3. Blood calcium determinations were within normal limits in the majority of the infants; in the others, with one exception, the amount of blood calcium was above the limit at which tetany usually occurs.

4. Electrical reactions were obtained on fifteen infants, and in all instances these were normal.

5. As Chvostek's facialis phenomenon is found in new-born infants without clinical, serologic or electrical evidences of tetany, it cannot be regarded as a pathognomonic symptom of this condition in early infancy.

# GASTRIC DIGESTION

## THE RELATION OF THE HYDROGEN ION CONCENTRATION VOLUME AND BUFFER CAPACITY OF THE GASTRIC CONTENTS TO A MILK TEST MEAL *

RAYMOND B. MILES, M.D.
BROOKLYN
AND
ALFRED T. SHOHL, M.D.
NEW HAVEN, CONN.

Studies in the chemistry of gastric digestion have centered about the acidity and action of the enzymes. It was early shown that in infancy a small amount of free hydrochloric acid is found in the gastric contents of the breast-fed infant, but none in those of artificially fed infants. No great progress was made until methods for measuring the hydrogen ion concentration were introduced. For the last twenty years, this has been the dominant interest in gastric analysis.[1]

Much of value lies in some of the older literature, a review of which, to 1908, was given by Clarke.[2] Motility was subject to measurement as soon as the Kussmaul tube was first used for infants by Epstein in 1880.[3] His observations were confirmed and extended by Leo,[4] who showed that breast milk passed out of the stomach more rapidly than cow's milk. As a possible correlation, he first described the "binding power" of milk for hydrochloric acid. Both these observations were soon confirmed by Einhorn,[5] who was probably the first in America to use the stomach tube to study gastric digestion in infancy. Escherich

* Received for publication, April 14, 1927.

* The experimental work done in this paper formed the material for the thesis presented by Dr. Miles for the degree of Doctor of Medicine, Yale University, 1924.

* From the Department of Pediatrics, and the New Haven Hospital, Yale University.

1. For a review of the literature see Babbott, F. L., Jr.; Johnston, J. A., Haskins, C. H., and Shohl, A. T.: Hydrogen Ion Concentration of Gastric Contents of Infants, Am. J. Dis. Child. **26**:475 (Nov.) 1923.

2. Clarke, T. W.: Gastric Digestion in Infants. A Review of the Literature, Am. J. M. Sc. **137**:674 (May) 1909.

3. Cited by Clarke (footnote 2).

4. Leo, H.: Ueber die Function des normal und kranken Magens und die therapeutischen Erfologe der Magen ausspülung im Säuglingsalter, Berl. klin. Wchnschr. **25**:981 (Dec.) 1888.

5. Einhorn, M.: The Time Required in the Stomach Digestion of Different Foods in Infancy, New York M. J. **50**:67 (July) 1889.

and Müller [6] then showed that cow's milk had a greater binding power than breast milk. This capacity of absorbing acid lies in part in the proteins and is increased by peptic digestion. A further advance was made by Hamburger and Sperk,[7] who stressed the fact that until the proteins are saturated with hydrochloric acid peptic digestion cannot take place. They added acid to gastric contents until hydrochloric acid was "free." The amount added they called the "acid deficit" of the gastric contents. This value plus the total acidity equals the "acid binding power" of the gastric contents, if no free hydrochloric acid is present. If free hydrochloric acid is present, the total acidity minus the free hydrochloric acid measures the "acid binding power."

The value is now called the buffer or buffer value, or "buffer capacity." Confusion has arisen from not clearly separating buffer capacity and the acid deficit.[8] We have employed the term buffer capacity to mean the amount of tenth normal hydrochloric acid required to change 100 cc. from $p_H$ 9.6 to $p_H$ 3.0, as conveniently measured by the two end points of the indicator, thymol blue. By total buffer we mean the buffer capacity times the amount, measured in terms of tenth normal solutions.

Our purpose in this study is to correlate the acidity, volume and buffer capacity of the gastric contents with milk test meals of varying volume concentration.

## PROCEDURE

To study the factors of gastric digestion, numerous observations were made on the same infants, rather than single or random determination on many subjects. Two infants, not acutely ill, but who were in the wards of the New Haven Hospital mainly as feeding cases, were employed in this study.

*History.*—H. K., a female infant, was about 8 months of age when the observations began, and about 10 months of age when they were discontinued. She was admitted because of moderate malnutrition, with possibly a slight degree of rickets, and during the first month of the period, during which gastric analyses were performed, suffered from a mild rhinopharyngitis. During her stay in the hospital, she was fed during various periods on whole milk formulas, liver soup, and butter-flour mixtures. She gained weight slowly, but improved markedly in general appearance during the period of observation.

M. N., also a female, was 6 months of age when the gastric analyses were begun, and about 8 months of age when they were discontinued. She was

6. Cited by Heubner, O.: Ueber das verhalten der Säuren wahrend der Magenverdauung des Säuglings., Jahrb. f. Kinderh. **32**:27, 1891.

7. Hamburger, F., and Sperk: Untersuchungen über die Magenverdauung bei neugeborenen Brustkindern., Jahrb. fur Kinderh. **62**:495, 1905.

8. Modern literature makes frequent allusion to the use of lactic acid to reduce the buffer value of cow's milk. Lactic acid is itself a buffer and the buffer capacities are additive, so that the addition of lactic acid increases the buffer capacity. Addition of hydrochloric acid does not increase or decrease the buffer capacity. The amount of hydrochloric acid necessary to bring the milk to a $p_H$ suitable for optimal digestion is, however, decreased. The "acid deficit" is diminished in both cases.

admitted because of a mild upper respiratory infection, with bilateral otitis media and a slight degree of rickets. During most of the period of observation, however, the infant was afebrile. Whole milk formulas were given during the first month of the observation, and liver soup during the last month. The gain in weight was satisfactory, and clinically the infant was much improved.

The infants observed in this study cannot be considered normal, for they were admitted to the hospital as feeding cases. However, at the time the observations were made, the infants were doing well and were gaining weight normally. The response to their test meals showed them well within the limits of our larger series[1] obtained not only from convalescent hospital cases, but also from "normal" infants in the Temporary Home. These data are not intended to establish normal values, for they are not sufficiently numerous nor can they be called normal. They were collected to show the mechanism of digestion in infants and to give comparison for the same infants with different test meals.

*The Test Meal.*—A milk meal, like the one used as by Babbott et al.,[2] was made by dissolving weighed quantities of Dryco, a partly skimmed dried milk preparation in distilled water. When prepared in the proportion of eight parts of the powdered milk to 100 parts of water, its composition corresponded to partly skimmed milk. The $p_H$ of this meal, determined electrometrically, was 6.25. It was found that 104 cc. of tenth normal solution was required to change the $p_H$ of 100 cc. of the meal from $p_H$ 3.0 to 9.6, which represents the buffer capacity.

It was intended to give meals of 100, 150, and 200 cc. in the proportions of 4, 8, and 12 parts of the powdered milk per hundred cubic centimeters of water. These were to be removed at intervals of thirty, sixty and ninety minutes. It was found, however, that the meal containing twelve parts of the milk powder per hundred cubic centimeters of water formed curds in the stomach which were too large to pass easily through the catheter used to empty the stomach; consequently, this test meal was discontinued.

Complete series of examinations for the eight parts of Dryco to 100 of water dilution with the 100 and 150 cc. test meals, at thirty, sixty, and ninety minute intervals, were made on both infants. Also a series with a 200 cc. test meal, in the proportion of four parts of Dryco to 100 of water, was completed on infant H. K. The test meal consisting of four parts of Dryco to 100 of water was given in 100 and 150 cc. quantities to both infants, and was extracted at thirty and sixty minutes. No ninety minute observations were made, due to the fact that with this dilute meal practically nothing was left in the stomach after one hour.

The assumption was made that all of the gastric contents were removed. Experiment[9] showed the error to be so small that it could not affect the validity of the conclusions drawn from the analyses.

The character of the contents varied from clear fluid to opaque material containing more or less mucus and fine curds. Blood was never present. In a few cases the contents were bile-tinged. These were rejected, as we wished to avoid cases showing known regurgitation of duodenal contents.

The infants were fed by bottle, if practicable, at least three hours after their last feeding, so that the stomach might be as empty as possible, and at the same time their feeding routine might be least interfered with. Digestion time was computed as the interval between the end of the experimental feeding and the removal of the gastric contents.

*Technic.*—The stomach contents were extracted by a soft rubber catheter and Dakin syringe. All the material that could be removed was withdrawn. No fractional studies were made. All apparatus was rinsed in distilled water.

---

9. Unpublished data. This was determined by washing out the stomach and estimating the total buffer.

The contents were measured and analyzed immediately after removal, or, if this was impossible, were placed in the refrigerator. Analysis was in no case delayed for more than four hours.

The samples were filtered through a Gooch crucible with an asbestos pad, mounted in a Witt filtering apparatus. All apparatus was washed free of acid and alkali with distilled water. The hydrogen ion concentration of the filtrate and the buffer capacity were determined colorimetrically, by the method of Shohl and King.[10] The buffer capacity determined on 1 cc. of the filtrate was the amount of tenth normal solution required to change the $p_H$ from 3.0 to 9.6. Titrations were made with a microburette calibrated in 0.01 cc. This figure was multiplied by 100 in order to express the buffer value as cubic centimeters of tenth normal solution per hundred cubic centimeters of contents. The "total buffer" present was found by multiplying the amount recovered in cubic centimeters by the buffer capacity per cubic centimeter.

TABLE 1.—*Averages from which Curves were Plotted*

| | $p_H$ | Vol. (Cubic Centimeter) | Buffer Capacity (Cubic Centimeter of Tenth Normal Solution) | Total Buffer (Cubic Centimeter of Tenth Normal Solution) | $p_H$ | Vol. (Cubic Centimeter) | Buffer Capacity (Cubic Centimeter of Tenth Normal Solution) | Total Buffer (Cubic Centimeter of Tenth Normal Solution) | $p_H$ | Vol. (Cubic Centimeter) | Buffer Capacity (Cubic Centimeter of Tenth Normal Solution) | Total Buffer (Cubic Centimeter of Tenth Normal Solution) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 8/100, 100 cc. | | 30 min. | | | | 60 min. | | | | 90 min. | | |
| Infant H. K..... | 4.5 | 54 | 44 | 24 | 4.8 | 47 | 53 | 25 | 4.5 | 30 | 46 | 14.6 |
| Infant M. N..... | 5.3 | 39 | 44 | 17 | 5.0 | 22 | 23 | 5.1 | 7.4 | 10 | 37 | 3.7 |
| Average of both infants..... | 4.8 | 46.5 | 44 | 20.5 | 4.9 | 44 | 38 | 15.2 | 4.8 | 20 | 41 | 9.1 |
| 8/100, 150 cc. | | 30 min. | | | | 60 min. | | | | 90 min. | | |
| Infant H. K..... | 4.6 | 45 | 64 | 28.8 | 4.7 | 45 | 49 | 22 | 4.6 | 45 | 35 | 16.1 |
| Infant M. N..... | 5.5 | 49 | 33 | 16.7 | 5.4 | 28 | 37 | 10.4 | 5.2 | 7 | 36 | 2.5 |
| Average of both infants..... | 4.9 | 47 | 48 | 22.8 | 4.9 | 36 | 43 | 16.2 | 4.8 | 15 | 35 | 9.2 |
| 4/100, 100 cc. | | 30 min. | | | | 60 min. | | | | 90 min. | | |
| Infant H. K..... | 3.9 | 24 | 54 | 13.4 | 6.6 | 4 | 20 | 0.8 | | | | |
| Infant M. N..... | 4.5 | 23 | 23 | 5.3 | 6.1 | 2 | 15 | 0.3 | | | | |
| Average of both infants..... | 4.2 | 23 | 38 | 9.2 | 6.3 | 3 | 17 | 0.5 | | | | |
| 4/100, 150 cc. | | 30 min. | | | | 60 min. | | | | 90 min. | | |
| Infant H. K..... | 4.3 | 37 | 52 | 19.2 | 4.1 | 13 | 31 | 4.0 | | | | |
| Infant M. N..... | 5.5 | 68 | 29 | 19.7 | 6.6 | 16 | 31 | 4.8 | | | | |
| Average of both infants..... | 4.6 | 52 | 40 | 19.4 | 4.4 | 14 | 31 | 4.4 | | | | |

It was found that the buffer capacities of the residue and of the filtrate were in close accord in a number of samples examined. Consequently, the filtrates were used in making the determinations because of the greater ease in working with clear solutions.

## RESULTS

To simplify the tables and charts, the various test meals used will be indicated by abbreviations. For example, $\frac{4}{100}$, 150 cc. will mean that a meal of 150 cc. has been given, in which the concentrations of Dryco was 4 Gm. of powdered milk per hundred cubic centimeters of distilled water. The results are given in table 1, from which the charts are drawn.

10. Shohl, A. T., and King, J. H.: Determination of the Acidity of Gastric Contents III; Combined Acidity and Buffer Value, Bull. Johns Hopkins Hosp. **31**:162 (May) 1920.

(A) RELATION OF TIME TO THE $p_H$ OF CONTENTS REMOVED

Chart 1 shows the curve of the hydrogen ion concentration, expressed as $p_H$, during the process of digestion. The $p_H$ of the test meals given was 6.25. The results are in agreement with the values in the literature and in addition show that the smaller and more dilute meals become more acid and in less time than the larger and more concentrated feedings. The marked decrease in acidity of the $^4/_{100}$, 100 cc. meal can best be explained by the fact that at the end of one hour, an average of only 3 cc. was removed from the stomach, and that this probably contained alkaline duodenal juice, regurgitated during the process of artificially emptying the stomach.

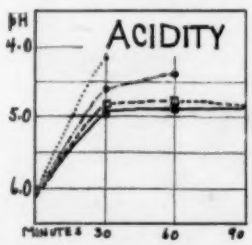



Figure 1

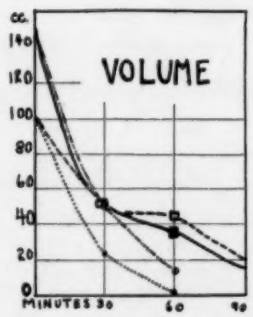



Figure 2

Chart 1.—Hydrogen ion concentration, expressed as $p_H$, during the process of digestion.

Chart 2—Average of the figures obtained in both infants, showing that the amount recovered decreases regularly with the digestion time.

(B) RELATION OF TIME TO THE AMOUNT RECOVERED

Chart 2, the average of the figures obtained for both infants, shows that the amount recovered decreases regularly with the digestion time. The dilute mixture leaves the stomach at a more rapid rate than the more concentrated mixture (table 2).

TABLE 2.—*Absolute Loss in Volume of Various Meals*

| Test Meal | 30 Min. No. Cc. Lost | 30 Min. Per Cent Lost | 60 Min. No. Cc. Lost | 60 Min. Per Cent Lost | 90 Min. No. Cc. Lost | 90 Min. Per Cent Lost |
|---|---|---|---|---|---|---|
| 4/100, 100 cc. | 76 | 76 | 97 | 97 | .. | .. |
| 4/100, 150 cc. | 98 | 65 | 136 | 90 | .. | .. |
| 8/100, 100 cc. | 54 | 54 | 56 | 56 | 80 | 80 |
| 8/100, 150 cc. | 102 | 68 | 114 | 76 | 135 | 90 |

After the large loss in volume during the first half hour of digestion, the more dilute $^4/_{100}$ test meals decrease in volume at a rate approximately twice that of the $^8/_{100}$ meals, which contain twice the amount of pow-

dered milk. Again, at the end of one hour, the dilute meal has lost more than 90 per cent of its initial volume, while the concentrated meal has lost only from one half to three fourths. Approximately 15 per cent of the volume of the more concentrated meal still remains at the end of one hour and a half, whereas digestion had been completed for the more dilute meal.

For the same concentration of milk, the loss in volume is greater in the case of the meals consisting of 150 cc. than in that of the 100 cc. meals. However, the amount leaving the stomach depends less on the concentration than on the volume of the meal. The $^{8}/_{100}$, 150 cc. meal loses more cubic centimeters during a given thirty minute period than does the $^{4}/_{100}$, 100 cc. meal. Volumes of feeding seems to bear a direct relation to gastric motility: when larger amounts are fed, larger amounts leave the stomach in a given time.

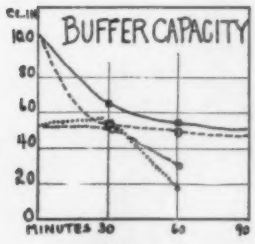



Figure 3

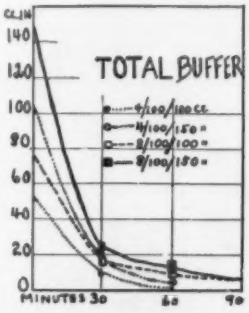



Figure 4

Chart 3—Average buffer capacity obtained with varying test meals.

Chart 4—Effect of digestion on the total buffer of the contents removed from the stomach.

### (c) RELATION OF TIME TO THE BUFFER CAPACITY OF THE CONTENTS

Chart 3 shows the average buffer capacity obtained with varying test meals. In the more concentrated test meals, the buffer value at the end of ninety minutes is nearly that which it was at thirty minutes, and at sixty minutes it is somewhat less than at either of the other two points. Since only 1 cc. of filtrate was used in determining the buffer values, the experimental error would indicate that this curve should be interpreted as a straight line. Consequently, no significance is attached to the drop at sixty minutes.

The $^{4}/_{100}$ test meals, on the other hand, show a definite drop in the buffer capacity at the sixty minute determination.

These data indicate that the buffer concentration of the gastric contents remains at a more or less constant level, and does not decrease until digestion is nearly accomplished.

### (D) RELATION OF TIME TO TOTAL BUFFER OF CONTENTS

Chart 4 shows the effect of digestion on the total buffer of the contents removed from the stomach. These figures were obtained by multiplying the number of cubic centimeters of contents removed by the value for the buffer capacity. These curves more truly represent the state of the digestion than either the volume or buffer capacity, because they are the resultant product of the two. They indicate clearly that digestion is more nearly complete in the dilute meals than in the concentrated milk mixtures. Smaller amounts of buffer substance remain in the stomach in a given time. In fact by this standard, digestion is more nearly complete in the dilute meals in one hour than in the concentrated meals in one and a half hours.

### (E) RELATION OF $p_H$ TO AMOUNT RECOVERED

The conclusions in this and the three subsequent paragraphs were obtained by making graphs (not included here) of the data to express the desired relation. The relation of the amount of gastric content to the $p_H$ indicates that, in general, the larger the amounts recovered, the less acid is the reaction, and the smaller the amounts, the more acid. Quite small quantities, on the other hand, those below 16 cc., are much less acid than slightly greater amounts and represent the end stage of digestion.

The two infants show slightly divergent curves. The contents of the stomach of infant M. N. become more acid for a given decrease in volume than do those of H. K. This probably indicates a more active digestion on the part of M. N.

The more alkaline $p_H$ values are due to a short interval between feeding and removal of the contents, to a large amount of feeding, to a more concentrated mixture, or to less active digestion.

### (F) RELATION OF $p_H$ TO BUFFER CAPACITY

The hydrogen ion concentration increases as the buffer capacity decreases. In other words, gastric contents having a high buffer capacity are less acid. The individual curves of the two infants again indicate a greater gastric motility on the part of M. N., since the buffer capacity in this case decreases more rapidly than in the case of H. K.

### (G) RELATION OF $p_H$, TO TOTAL BUFFER

The greater the total buffer of the contents, the less acid will be their reaction, and vice versa. The curves for the two infants are again somewhat divergent and, as in the previous case, indicate a more active response of the stomach to changes in the meal for M. N. than for H. K.

The low total buffer values are found associated with the less acid contents. These contents were small in amount, and this is additional evidence that they represent completely digested meals with duodenal regurgitation.

### (H) RELATION OF BUFFER CAPACITY TO AMOUNT RECOVERED

A high buffer capacity is found in conjunction with a relatively large amount of gastric contents, and a low buffer value with a small amount of contents. High buffer capacities are a sign that digestion is not yet complete, and, conversely, when it is found that only small amounts of the contents of the stomach remain, their buffer capacity is low. Furthermore, the food tends to remain in the stomach at a high buffer concentration until gastric digestion is complete.

## COMMENT

The problem of gastric digestion involves the amount of acid juice secreted in response to meals of various concentrations and volumes, the amount of fluid secreted by the stomach, the effect of gastric digestion on food that passes into the pylorus, and the relation between the food in the stomach and that leaving it.

Carlson [11] states that gastric juice of a relatively low acidity is constantly being secreted during fasting. He also states that the more rapid the secretion of the gastric juice, the higher is the acidity, and the lower its pepsin content. The work of Pawlow and Cannon and their co-workers on the effect of food on the gastric secretion he considers inconclusive, and states that more evidence is needed on this subject.

Gorham [12] has suggested a method for determining the extent of dilution in gastric analysis. He differentiated that part of the gastric contents which represents the test meal from that part consisting of gastric juice. The method involves the addition of a measured amount of phenol red to the Ewald test meal, and colorimetric determination of the concentration of dye present in a filtered sample of the removed gastric contents. This method was tried, using both phenol red and thymol blue as indicators, in conjunction with a Dryco and water test meal. It was found, however, that a varying and often large proportion of the dye remained in the residue on filtration, and that even repeated washings with hot water and alcohol failed to remove it. This indicated such a large source of error that the method was not employed.

---

11. Carlson, A. J.: Secretion of Gastric Juice in Health and Disease, Physiol. Rev. **3**:1, 1923.

12. Gorham, F. D.: The Factor of Dilution in Gastric Analysis, J. A. M. A. **81**:1738 (Nov. 24) 1923.

Our method was selected because it was thought that if the $p_H$, the buffer capacity, and the amount of gastric contents were known, as well as the volume, concentration, $p_H$ and buffer value of the test meal, the volume of hydrochloric acid which had acted on it could be calculated. The total amount of fluid added by the gastric secretion could also be determined. Such calculations have been made by Arrhenius.[13] In the stomach, however, from which unknown amounts of material of undetermined composition are constantly being evacuated, it is impossible to calculate accurately the exact amount of gastric secretion. This phase of the problem will, in all probability, have to be solved by animal experimentation, in which the entire products of digestion can be removed as they leave the stomach.

It has been possible, nevertheless, to determine the normal reactions of the stomach to varying amounts and concentrations of feeding as digestion progresses. These facts are not only of theoretical but also of definite practical importance in their application to infant feeding.

From the data presented, it is evident that the more dilute the feeding, the more rapid is its rate of evacuation by the stomach, and in consequence, the more easily does gastric digestion proceed. This is in agreement with the observations of Clarke,[14] who stated: "The motility of the stomach is in inverse ratio to the concentration of the food." In fact, it appears that the 4/100 mixtures leave the stomach at a rate nearly double that of the 8/100 meals, which contain twice the amount of powdered milk. These results are closely paralleled by those found in determining the total buffer value in relation to the time elapsed. Here also the dilute meals lost in total buffer at a rate nearly double that of the more concentrated feedings. In this case, the amount recovered, being a function of the total buffer, is the most important determination, for it shows not only the volume digested but also the protein and salts removed.

At a given concentration, the larger the volume of the meal, the more rapidly does it leave the stomach. In this calculation, no account has been taken of the gastric juice secreted. If the amount of juice is the same in all cases, the relative volume relationships are as here presented. If, however, as has been shown, the volume of the gastric juice secreted is increased with larger meals, the effect of volume on evacuation rate is still more marked. Therefore, these data corroborate the opinion of Carlson that the motility of the stomach is an important factor in gastric digestion and that larger volumes pass through the stomach at a more rapid rate than do the smaller.

---

13. Arrhenius, S.: Quantitative Laws in Biological Chemistry, London, 1915, pp. 164.

14. Clarke, T. W.: The Effect of Certain So-Called Milk Modifiers on the Gastric Digestion of Infants, Am. J. M. Sc. **137**:872 (June) 1909.

The buffer capacity of the contents remains at approximately the same point, during their presence in the stomach, until digestion is nearly accomplished. The 4/100 feedings, in which digestion is practically complete at sixty minutes, show a drop in buffer value, whereas the 8/100 meals, in which digestion is slower, do not show a decrease even at the expiration of ninety minutes.

The hydrogen ion concentration of the more concentrated feeding was found to increase only slightly as time progressed, closely paralleling the curve of the buffer value. In the more dilute 4/100 feeding, on the other hand, the increase in the hydrogen ion concentration is more pronounced. The curves for the 8/100 meals indicate that the acidity is less at all times than is the case in the more dilute meals. The higher buffer of the more concentrated meals makes it necessary for the stomach to secrete a larger amount of hydrochloric acid in order to change the $p_H$. While the acidity of the 8/100 meals did not, during the period of digestion studied, reach as great a hydrogen ion concentration as the 4/100 meals, the total amount of acid secreted by the stomach was greater.

It has been shown that during digestion the stomach contents become progressively smaller and more acid. Marriott and Davidson [15] observed that a larger proportion of the feeding could be removed in two hours from those infants having a deficiency in gastric acidity than from those in whom the gastric juice was normal. This, in different terms, means that the greater the acidity of the contents, the smaller was the volume present, and our observations corroborate theirs in this respect. The authors state that, in their opinion, the hydrogen ion concentration is not the only factor influencing gastric motility.

Davidson [16] has shown a definite increase in the acidity of contents removed as the time between feeding and removal is increased. This point is also conclusively demonstrated by the work of Babbott et al.[1] as well as by the present study. Therefore, other factors being constant, it must be concluded that contents of a higher acidity leave the stomach at a more rapid rate than those less acid.

Our results have shown that for all except the smallest and most dilute meal the buffer concentration remains nearly constant during the height of digestion. Only when digestion is nearly complete in all meals does this value become diminished. This is even more convincingly shown with the experiments on gastric digestion in dogs,[17] in which

---

15. Marriott, W. McK., and Davidson, L. T.: Studies on Hydrogen ion Concentration of Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

16. Davidson, H.: Beitrag zur Physiologie u. Pathologie der Magenverdauung bein säugling, Arch. f. Kinderh. **69**:239 (April) 1921.

17. Standish, W. A.; Cowgill, G. R., and Shohl, A. T.: Am. J. Physiol. **81**: 696 (Aug.) 1927.

the buffer capacity increases at the height of digestion. It also confirms the observations of Hamburger and Sperk.[7]

Our observations are interpreted to mean that the more fluid portions are digested first and the more solid particles remain until the end of gastric digestion, of which the diminished sugar concentration of gastric contents is further evidence.

"Buffer capacity" has been used as a measure of concentration. This is only permissible in the absence of other factors. The buffer value may be increased by peptic digestion and by formation of weak acids, such as lactic acid. However, peptic digestion in the stomach of infants is negligible, and lactic acid formation almost never occurs in significant amount. The amount of fat split in the infant's stomach is also negligible as to its buffer capacity. The buffer capacity of the gastric juice is so much smaller than that of the meal used that it is unimportant.

Large meals, of a high buffer value, are the most difficult for the infant to digest, and require both a larger amount of gastric juice and a longer period in the stomach than do the more dilute mixtures.

## SUMMARY

It may be stated that those meals combining small volume with a relatively low concentration of buffer substances are the most easily digested. Such meals, even though their initial hydrogen ion concentration is the same as that of a more concentrated meal, require a smaller quantity of acid gastric juice to bring them to the $p_H$ optimal for digestion.

Therefore, in cases having a limited secretion of hydrochloric acid, the more dilute whole milk mixtures, containing the same amount of solids, are more easily digested.

## CONCLUSIONS

1. Dilute feeding mixtures leave the stomach at a more rapid rate than do those of greater concentration.

2. The hydrogen ion concentration of the stomach contents increases more rapidly with a dilute food than with a more concentrated milk of the same volume. The total acid secretion of the stomach is greater for the concentrated food of the same volume.

3. The decrease in total buffer of stomach contents at a given time is much greater in dilute than in the same amount of more concentrated mixtures.

4. The buffer capacity of the stomach contents remains high until digestion is nearly completed.

5. The hydrogen ion concentration of gastric contents is relatively low when there is a short digestion period, a slow digestion, a large

amount of feeding, or a concentrated mixture. The $p_H$ is a result of at least these four factors.

6. Stomach contents with a high total buffer have a low hydrogen ion concentration; those with a low total buffer value are found to have a relatively high hydrogen ion concentration when compared after the same digestive period.

7. In stomach contents in which the hydrogen ion concentration is high, the buffer value is low; in those with less acid values the buffer value is high, except at the end of digestion.

8. When large amounts of gastric contents are associated with high buffer capacity, digestion is incomplete.

9. The study of the buffer value of gastric contents in conjunction with measurement of $p_H$ and volume offers a new means of studying gastric digestion.

# MUSHROOM POISONING DUE TO HEBELOMA CRUSTULINIFORME

## REPORT OF FOUR CASES *

H. W. PRICE, M.D.
BALTIMORE

*Hebeloma crustuliniforme* (Bulliard) Fries has long been considered a poisonous mushroom both in Europe [1] and in America,[2] but the toxicity of the American member of the species has been a matter of doubt.[3] A careful search of the literature has revealed no case of poisoning by ingestion of this mushroom in America. Experimentally, Ford [4] has shown that "it contained a small amount of hemolysin, no agglutinin, and had no demonstrable toxic action on rabbits, guinea-pigs, or on the exposed frog's heart."

### REPORT OF CASES

On Oct. 26, 1926, a Russian family of four, in Baltimore, partook of a supper consisting chiefly of a mushroom stew. The mushrooms had been gathered by the father on the afternoon of the previous day on the outskirts of the city and were supplemented with market vegetables. The family had been in the habit of obtaining an occasional mushroom supper in this manner in Russia, where they were acquainted with their local poisonous and nonpoisonous types. They made no claims to immunity from mushroom poisoning and were unacquainted with the relative immunity to poisoning with *Amanita muscaria* possessed by the Korak tribe in Siberia.[5] Although the chief means of support of the family was bootlegging, careful questioning ruled out the possibility of poisoning from alcoholic beverages. The other articles of diet were all fresh common market products. The meal was eaten about 7 p. m. It was observed that the stew had an unusual taste, but average portions were eaten by all. By 7:30 p. m., all four had become exceedingly drowsy and passed into coma which lasted till about 9:00 p. m. They were then simultaneously aroused by severe attacks of abdominal cramps accom-

---

* Received for publication, March 8, 1927.

* From the Harriet Lane Home of the Johns Hopkins Hospital.

1. Ford, W. W., in Legal Medicine, Peterson, Haines and Webster: ed. 2, Philadelphia, W. B. Saunders Co., Vol. 2, pp. 817-857, 1923. Stevenson, J.: British Fungi, Edinburgh and London, Wm. Blackwood & Sons, vol. 1, p. 260, 1886. Swanton, E. W.: Fungi and How to Know Them, London, Methuen & Co., p. 127, 1909. McIlvaine, C.: One Thousand American Fungi, Indianapolis, The Bowen-Merrill Co., p. 287, 1900.

2. Clements, F. E.: Minnesota Mushrooms, Minnesota Geological and Historical Survey, Minnesota Plant Studies no. 4, Univ. of Minn., pp. 63-64, 1910. Atkinson, G. F.: Mushrooms, Edible and Poisonous, ed. 3, New York, Henry Holt & Co., p. 157, 1911. Patterson, F. W., and Charles, V. K.: Bull. U. S. Dept. of Agric., no. 175, April 29, 1915. Kauffman, C. H.: The Agaricaceae of Michigan (Publication no. 26, Biol. Series no. 5), Lansing, Mich., Geol. and Biol. Surv., vol. 1, pp. 470, 476, 477, 856, 1918.

3. Footnote 1 (fourth reference). Footnote 2 (first and fourth references). Ford, W. W.: J. Pharm. & Exper. Therap. **6**:206 (Nov.) 1914.

4. Footnote 3 (third reference).

5. Footnote 1 (first reference).

panied by diarrhea. The stools were profuse but without blood. The father, aged 33, continued to have cramps, tenesmus and diarrhea for three days, but did not vomit. The mother, aged 29, had a severe attack of vomiting with the onset of the abdominal cramps; and cramps, tenesmus and diarrhea lasted till the evening of the following day. The daughter, aged 11 years, vomited four times during the night, and was so prostrated with cramps, tenesmus and diarrhea that the following forenoon she was brought to the Harriet Lane Home Dispensary. The son, aged 10 years, vomited once during the night, but the following morning his tenesmus and diarrhea were not sufficient to prevent him from going to school. No hematemesis was observed. There were no oliguria, anuria, delirium, hallucinations, convulsions, excitation, jaundice, anemia, or hemoglobinuria. The symptoms of stupor and coma preceded the gastro-intestinal symptoms. When the patients were first seen, the only physical signs were those incident to acute indigestion. There were no sequelae.

## COMMENT

Only a small portion of the mushrooms gathered were used in the stew. The remainder were identified by Mr. Louis C. C. Krieger. The only questionable species found was *Hebeloma crustuliniforme*. However, a number of the mushrooms were decomposed, and some had been frozen.

Ford [5] has suggested a new classification of mushroom poisoning. Mycetismus gastro-intestinalis, in which the symptoms are mainly nausea and diarrhea, is caused by *Russula emetica,* etc. Mycetismus choleriformis, in which the symptoms are at first gastro-intestinal followed by collapse and anuria and characterized by a high mortality, is due to the ingestion of *Amanita phalloides*. Mycetismus nervosus, in which the gastro-intestinal symptoms are followed by delirium, hallucinations, convulsions and coma, is produced by *Amanita muscaria* and some of the *Clitocybes, Inocybes* and *Boleti*. Mycetismus sanguinareus which is differentiated by jaundice, anemia, and hemoglobinuria, is caused by *Helvella esculenta*. Mycetismus cerebralis, in which the symptoms are transient excitement and hallucinations, is due to *Paneolus papilionaceus* and *Paneolus campanulatus*.

While the symptoms of the four patients presented are mainly those of mycetismus gastro-intestinalis, which may have been due to the decomposed and frozen mushrooms, yet the stupor and coma and the close relationship between the *Hebelomas* and the *Inocybes* and *Boleti* [6] would suggest that mycetismus nervosus was also present and that it was caused by *Hebeloma crustuliniforme*.

6. McDougall, W. B.: A Handbook of Mushrooms, Boston and New York, Houghton Mifflin Co., p. 151, 1925.

# Progress in Pediatrics

## EVIDENCE OF RICKETS PRIOR TO 1650*

JOHN A. FOOTE, M.D.
WASHINGTON, D. C.

When Whistler published his slim Leyden graduate thesis on rickets in 1645, which was followed by Glisson's adequate volume in 1650, the origin of what was then called "an entirely new disease" was attributed to conditions having little relation to diet and sunshine. But, by the end of the eighteenth century, authorities were able to conclude that climate and especially dampness had much to do with the origin of rickets, and that improper food also had some part in its etiology.

From the time of the first description of this malady, the theory that rickets was an inheritable ailment has persisted with singular tenacity. The influence of maternal heredity still claims attention, even though modern experimental science seems to have proved that the disease is a disturbance of calcium and phosphorus metabolism caused by lack of a mysterious substance in the diet and a lack of sufficient sunshine on the surface of the body. The theory that it is a purely inheritable condition has not been substantiated by the animal experiments conducted by Hess and Weinstock.[1] The hypothesis of Schmorl,[2] that rickets is a manifestation of a deficient mineral deposit at birth, which is shown in some infants to a greater degree than in others and which is most marked in those prematurely born, served to revive the persistent and recurring idea that maternal influence in the production of rickets is not negligible even though the disease may not be strictly inheritable. The fact that rickets was found in nursing infants of Central Europe to a marked degree after the late war, and especially in regions in which food shortage and dietetic imbalance had prevailed among the civilian population, served to focus attention on the implication of a maternal rôle in the production of this disease. Suggestive recent work of Mitchell, Greenbaum et al,[3] would indicate that, while nearly all children ultimately develop incipient rickets, infants born of mothers who were fed on a low and insufficient caloric ration develop a type of the disease which is unusually resistant to the ordinary methods of treatment.

* Received for publication, June 29, 1927.

1. Byfield, H., and Daniels, Amy L.: The Rôle of Parental Nutrition in the Causation of Rickets, Tr. Sect. Dis. Child. A. M. A., 1923, pp. 55-62.

2. Schmorl: Arch. f. exper. Path. u. Pharmakol. **73**:313, 1913.

3. Greenbaum, J. V.; Selkerk, T. K.; Otis, F. A., and Mitchell, A. G.: Effects of Diet During Pregnancy on Development of Rickets in the Offspring, J. A. M. A. **87**:1108 (Oct. 2) 1926.

Insufficient or improper diet and insanitary housing conditions among the entire population are common occurrences during and after wars, especially in countries overrun by armies and when disease and famine come in the wake of war's destruction.

If one accepts the now well proved hypothesis that rickets is a disease of mineral metabolism caused by a lack of certain substances in the diet or by a lack of sufficient sunshine, especially in industrial cities in northern countries, and that war, famine and disease predispose populations to its ravages, one is postulating conditions some of which have occurred over and over again throughout the world, among both civilized and uncivilized peoples in various periods of history.

When one considers the conditions enumerated in connection with the historical proof of their prevalence in past times, one sees no reason why rickets should not have existed before 1650, and one may be certain that it did so exist and has existed, perhaps from the beginning of time.

### THE EVIDENCE OF SWADDLING

Swaddling the new-born infant was a custom among all peoples of antiquity except the Spartan Greeks and the Egyptians. That it was frankly a procedure adopted as a preventive of deformities is attested by practically all the ancient authors who have referred to the practice. The almost universal prevalence of this custom among widely separated peoples would seem to be good presumptive evidence that deformities were not uncommonly seen in older children among most of the nations of Europe from the beginning of history. Written proof is found in the second century A. D.[4]

Soranus of Ephesus says (chapter XXXIX): "Since swaddling is an important reinforcement and a preventive of deformities, it is best not to free the infant from its protection until the body has become strong enough to remove all fear of the appearance of irregularities of form." He says again, in chapter XL, to which Findlay has called attention: "The infant's feet may become crooked from unwise attempts at walking. Frequent examples of such deformity are seen in Rome, due in most cases to ignorance and improper care of the infant. City women devote much less time and care to their infants than those in the rural districts, hence the more frequent occurrence of these deformities among the infants of city dwellers. Yet there are some who regard deformities as the result of colds, sex defects of parents, or conception while one or other parents are intoxicated."

---

4. Troitski, I. V.: Sorani Ephesius (In Russian), Keiv Press of Imperial University of St. Vladmir; unpublished translation by J. Ohsohl and J. Foote. Rose, V.: Sorani Gyllaeciorum (Greek text), Leipzig, 1882, chapters XXVI-XLXI, pp. 248-292.

Acquired deformities of the bones in remote times could exist not only among civilized peoples but also among uncivilized as well, when the conditions favorable to their production were present. It has been asserted that not even presumptive evidence of rickets has been found in the bones of precolumbian Peruvian children. It is possible that the statement is true of the bones of infants, for it would be easy to see how such bones would not stand the ravages of time so well as completely ossified bones.

Contrary to this assertion, the Osteological Collection at the U. S. Army Medical Museum in Washington, which is in charge of Dr. A.

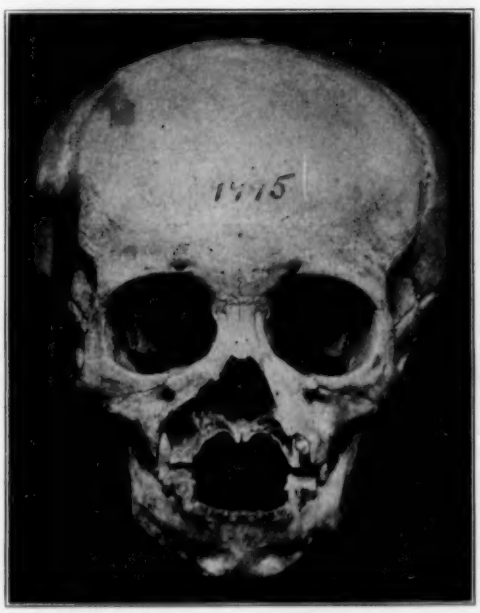



Fig. 1.—Skull of child, aged about 5, from an ancient cemetery (Chicana Valley, Peru), showing rickets and probably syphilis. From the U. S. Army Medical Museum.

Hrdlicka, contains a skull of a precolumbian boy, from Peru, who was about 5 years of age. This skull, which is typically rachitic, is labeled "rickets and probably syphilis" (fig. 1).

In all probability, rickets existed among the tribes of northern Indians, but mound burial is not kind to cartilaginous bone, and the evidence is not abundant. However, in the U. S. Army Medical Museum is also a deformed radius of a youth, aged about 19, which is labeled "Deformity of radius, probably due to rickets" (fig. 2). The bone was sawed through to assist in making the diagnosis.

### RICKETS AND CHONDRODYSTROPHY

Much has been said about the absence of representations of rickets in ancient painting, when compared with the frequently encountered pictures of chondrodystrophic dwarfs. But it must be remembered that the rachitic person is never so grotesque as the chondrodystrophic person, and that the dwarfs whose portraits survive were usually painted because they were court attendants or buffoons, and therefore people of importance. Only portraits of important persons were painted in olden times. Practically no paintings were made of children as children, until within the last 200 years. Pictures of children as princes, or nobles, or as saints or gods exist without number, and such figures were always idealized. Painters would never consciously represent imperfect creatures unless they were especially commissioned to do so, or were in search of the grotesque, as in the case of the cretinoid and hydrocephalic dwarfs and the idiots of Valesquez, or in Ruben's picture of a microcephalic dwarf in his painting of Count Thomas Arundel and his wife. Certainly they would not take imperfect creatures for their

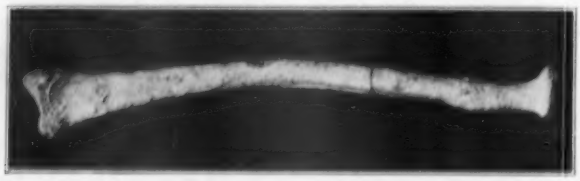


Fig. 2.—Right radius of Indian boy, aged 19, from precolumbian burial place (no. 9, Calhoun, Ky.), showing the outward curvature suggesting early rickets. From the U. S. Army Medical Museum.

models when they wished to depict supernatural characters; and the depicting of supernatural characters was the chief concern of art among the old masters. However, if rickets was prevalent, it is reasonable to suppose that primitive artists might unconsciously represent it, believing that it was normal for infants to have square heads, pot bellies and grooved chests.

### ECONOMIC STRESS AND INDUSTRIALISM IN THE FIFTEENTH CENTURY

The fifteenth century saw the rise of primitive religious art in Central Europe. This was especially true of Germany and the Netherlands. In the latter half of the previous century, the terrible Black Death had ravaged the population of all Europe to a degree surpassing any previously recorded plague. Recurrences came after the original visitation, and in the fifteenth century, the populations of Central Europe had scarcely recovered from the terrible scourge. With the passing of feudalism came industrialism; people began to congregate in cities, such

as Cologne, Bruges and Nuremberg, where weaving, metal working and other industries were developed. By 1475, Cologne was an important center of the great Hanseatic league which had been formed for purposes of trade. Nuremberg was a member of the Schwabian league, and Schwabia, after many civil struggles between the burghers and the

Fig. 3.—"Adoration of Christ by Mary" by Master of the "Life of Mary," Cologne (1460), showing Harrison's groove and protuberant abdomen.

margraves in its cities, and between rival petty rulers of neighboring towns, was policed by a large army. The peasant uprisings throughout Germany had begun and had been put down with great cruelty. City fought with city, and a disastrous war was waged by Germany against Hungary, in which Emperor Frederick II was defeated.

Especially in the last half of the fifteenth century did ideal conditions exist for the production of rickets—an industrial population living in crowded, walled cities, a northern climate under unhygienic conditions, and the effect of warfare on a society that would be poorly adapted to healthful life in cities even under far more favorable conditions than prevailed in those days. It would be natural to look for evidence of this disease among the people who lived in Cologne and Nuremberg and

Fig. 4.—"The Nativity" by the Suabian Master of Augusburg (1470), showing square head of rickets in cherubim.

Bruges between 1450 and 1500, or from a century and a half to two centuries before Glisson described the disease in England. Fortunately, the painters of that period made many pictures of religious scenes in which children were used as models, and one can call on that inspired school of painting which flourished so wonderfully in the unsettled years after the middle of the fifteenth century for clinical material. Correspondingly, in the pictures of the second half of the sixteenth century

one sees a great many well nourished children and fewer rachitic children, despite the fact that rickets appeared in England a century later. One subject favorable for the purposes of this study was also a favorite with primitive religious painters—"The Adoration of the Child," in which the the Infant was shown lying on the floor entirely naked.

Fig. 5.—"The Holy Family" by Bernhard Strigel of Nuremberg (1485), showing square head, Harrison's groove and other stigmas.

Among the fifteenth century painters of the Netherlands and Germany whose works I have examined, the following show clinical rickets in the infant: 1447, Stephen Lochner, "Virgin in the Grove of Roses," in the Cologne-Richartz Muzeum; 1460, Master of the "Life of Mary"; "Adoration of the Child," (fig. 3), Cologne-Richartz Museum; 1470, Swabian Master (of Augusburg) "Adoration of the Child," in Augus-

burg Church of St. Moritz, also "The Nativity" (fig. 4) and the "Adoration of the Magii" in the Maximillian Museum. A number of other of his pictures show the children with the stigmas of rickets: In 1485, Bernhard Strigel of Nuremberg, "The Holy Family," in the Germanic Museum, Nuremburg (fig. 5); 1490, Michael Pacher of

Fig. 6.—"The Nativity" by Michael Wohlgemut of Nuremberg (1480), showing deformities of head and chest, with protuberant abdomen.

Nuremberg, "Birth of Christ," St. Wolfgang Church; 1479, Michael Wohlgemut of Nuremberg, "Birth of Christ"; Zwicau, Marien Kirche (fig. 6); 1500, Albrecht Durer, Nuremberg, "Madonna with the Siskin." In this painting the infant holds a flour-ball in his hand. Hans Bergmaier, sixteenth century painter, also depicted rickets (fig. 7).

Among the Netherlands painters are Bruges Master, 1440, "Adoration of the Magi," Bruges Museum; 1440, Rogier Van Der Weyden, Brussels, "St. Luke Painting the Madonna," Alte Pinekotheck, Munich; 1490, Dirk Bouts, Harlem, "Virgin and Child," National Gallery, London.

Fig. 7.—"Virgin and Child" by Hans Bergmaier, of Nuremberg (1500), showing rachitic head and bow legs.

The last painting shows a splendid clinical picture of Harrison's groove (fig. 5).

The evidence of these artists, who painted what they saw, seems indisputable. There is now no reason, in view of what is known of its causes, to say that rickets is or must be a disease exclusively of even remotely modern times, or that it is a disease called into existence by

the peculiar conditions of life in modern civilized communities. Rickets undoubtedly existed to some extent at all times and periods of the world's history, and in many countries evidence found in painting suggests that it was a common condition in the industrial cities of Germany and Holland [5] at least 200 years before its description by Glisson, and such evidence is confirmatory of the present day theories of its etiology and pathogensis.

---

5. Heidrich, Ernst: Die Kunst in Bildern Die Alt Deutsche Malerei, Jena, 1910; Die Alt Niederlandische Malerei, Jena, 1910. These works contain reproductions of many paintings mentioned in the text.

# News and Comment

## RESOLUTIONS ADOPTED BY CHILD WELFARE COMMITTEE OF LEAGUE OF NATIONS

The following resolutions were adopted by the Child Welfare Committee of the League of Nations in its Third Session, May, 1927.

I: The Child Welfare Committee has considered the resolution of the assembly asking it to continue its enquiry into the cinema in relation to child welfare, and requests the council to ask the governments to furnish information on the lines of the questionnaire which it has drawn up.

1. Could any arrangements usefully be made for the exchange of information between different countries in regard to films which are good or bad for children and young people?

2. Can any facilities be given for the better international circulation of films which are specially suitable for children, for either instruction or amusement?

II: The Child Welfare Committee notes with gratitude the efforts of the Health Committee to improve and standardize statistics regarding still-births and infant mortality, and thanks it for the cooperation offered in the study of the protection of early childhood. The Child Welfare Committee relies on it to study the medical aspects of the question, and requests it to forward to the Child Welfare Committee the documents dealing with all social aspects of the question which concern child welfare.

III: The Child Welfare Committee considers that it is not necessary, at any rate for the present, to send a questionnaire to the governments on the question of the mental and physical recreation of children.

It decides to retain on its program this question, the importance of which it fully appreciates.

The committee appoints Dame Katharine Furse, Dr. Matz and Dr. Humbert to act as rapporteurs. Their report, which will be examined at the next session, should mention the methods adopted in different countries and the results already obtained. The committee would be grateful to the International Labour Office if the latter would communicate to the secretariat any information it may possess regarding the utilization of workers' spare time in its relation to child welfare.

IV: The Child Welfare Committee thanks the International Labour Office for its valuable report. The committee considers that, while the evidence afforded by the report as to the effect of the family allowance system on the well-being of children is not sufficient to justify definite conclusions, it is sufficiently favorable to justify the committee in asking the International Labour Office to continue its investigations and to furnish the committee with a further report at its next meeting.

V: The Child Welfare Committee has made itself acquainted with the replies to the questionnaire framed by the Legal Sub-Committee on the two draft conventions dealing with the relief and repatriation and with the execution of judgments relating to maintenance which have been received from the governments of Belgium, the United States of America, France, Great Britain and Roumania, and from the International Labour Office, the International Child Welfare Association and the Save the Children Fund International Union.

The committee decided to request the states represented on the committee which have not yet answered the questionnaire to do so as soon as possible.

The secretariat should point out to the governments concerned that the object of the second draft convention is in a general manner to insure by every

practicable means the fulfilment by parents of their obligations toward their children from whom they are separated.

As soon as a certain number of answers from the governments have been received by the secretariat, the Legal Sub-Committee will be convened in order to make a general and thorough study of these answers and report thereon to the Child Welfare Committee.

VI: 1. The Advisory Commission, sitting as a plenary meeting of the two committees, has taken note with the greatest interest of the report submitted to the Child Welfare Committee on the legal age of marriage and the age of consent.

2. It is of opinion that this question should continue to be examined jointly by the two committees, since the problems which it involves are concerned both with the traffic in women and children and with child welfare.

3. The commission, being convinced that the fixing of too early an age as the age of consent is likely to encourage traffic in women and children and to lead to the corruption of young persons, requests the Council of the League of Nations to draw the attention of governments to the imperative need of fixing the age of consent sufficiently high to insure the effective protection of children and young people.

4. As regards the legal age of marriage, the commission also thinks that it is important that the age of marriage should reach an adequate standard. It decided to postpone to its next session further consideration of this question and its possible relation to the age of consent.

VII: The Child Welfare Committee, bearing fully in mind the council's observations on the question of juvenile courts, instructs the secretariat to await the results of the inquiry now being conducted by the International Prison Commission on this question, and to submit a report at the next session.

VIII: The committee thanks M. Martin for his report on blind children, and hopes that this example will encourage other delegates and assessors to make similar reports.

The committee decided to keep the question on its agenda, and, with a view to completing the information at its disposal, would be glad to receive, before the next session, similar reports from members and assessors, and also from any specialized associations which the secretariat may approach with this object in view.

The members of the committee are asked to study and to submit information on the problem of blind children under the following headings:

1. Statistics and causes.

2. Assistance to blind children.

3. Education of blind children.

4. Training of blind children and the occupations for which they are suited.

The committee would also be glad to receive any information which the International Labour Office may be able to furnish on the fourth paragraph.

IX: The Child Welfare Committee, having decided to make a study of the position of the illegitimate child, requests the council to instruct the secretary-general to send the questionnaire it has prepared to all states.

1. What are the rights and obligations of the mother and of the father toward the illegitimate child?

2. Is action to establish the paternity of the child allowed (affiliation proceedings)? If so, how is this action undertaken?

3. What conditions govern the legitimization of illegitimate children?

4. What rights do illegitimate children possess to claim maintenance from their parents?

5. What are the rights of inheritance or succession of illegitimate children?

6. Is there a system of official guardianship for illegitimate children? If so, how is this guardianship organized?

7. Are there any other means, and, if so, of what nature, provided either by the laws or by institutions for insuring the moral and material protection of illegitimate children?

## POSTGRADUATE LECTURES IN PEDIATRICS

A series of postgraduate lectures in pediatrics will be given by Dr. P. F. Armand-Delille and Dr. B. Weill-Halle during the first and second weeks of October of this year. The lectures will be held in the School of Pediatrics of the Faculty of Medicine, 64, Rue Desnouettes, 15°; at the Hospital Hérold, Place du Danube, 19°, and at the Hospital de la Charité, 47, Rue Jacob, 7°, Paris.

The lectures will cover all phases of pediatrics, particularly tuberculosis in children.

## COURSE IN PUERICULTURE

A course in puericulture has been instituted by the Italian Red Cross under the directorship of Professor Vagalussa. The course will include the following subjects: alimentation of infants; infectious diseases; orthopedic surgery; radiodiagnosis and radiotherapy; medical gymnastics; neuropsychiatry and social legislation.

## CONGRESS OF FRENCH PEDIATRICIANS

The fifth Congress of French Pediatricians will be convened at Lausanne on Sept. 29, 1927, under the direction of Dr. J. Taillens, clinical professor of diseases of children in the university of that city. Subjects for discussion at this meeting will be poliomyelitis and bronchopneumonia.

## DEATH OF PROFESSOR SARGENTE

Prof. Pasquale Sargente, founder and director of the "Ospedale Infantile Tiburtino" in Rome died recently. He occupied a prominent place among Italian pediatricians and has made numerous contributions to pediatric literature.

## DEATH OF DR. GUIDA

G. Guida recently died in Florence, Italy. He was a pioneer in Italian pediatrics. He founded and controlled the "Ospedale Meyer" and "Instituto degli Innocenti." He wrote considerably on the subject of practical puericulture.

## ANNUAL CONVENTION OF AMERICAN HOSPITAL ASSOCIATION

The twenty-ninth annual convention of the American Hospital Association will be held in Minneapolis on Oct. 10 to 14, 1927.

# Abstracts from Current Literature

## Pathology, Bacteriology and Biochemistry

A Contribution to the Study of Merbaphen (Novasurol) in Children. R. Baranski and M. Bussel, Rev. franç. de pediat. **2**:736, 1926.

According to Politzer and Stolz, every person has a certain amount of "residual water" which may be measured by the loss in weight in twenty-four hours following the injection of merbaphen. It is said that merbaphen has a marked diuretic action, and that after an injection of merbaphen the swelling property of colloids is diminished. Taking careful account of the fluid intake and output, the effect of merbaphen on various children was determined. The authors conclude that the merbaphen test applied to normal children is of no value, and that its diuretic action on normal children is relatively rare. The children tested could be divided into three groups: (1) those on whom merbaphen had no effect; (2) those in whom it had a diuretic action provided no water was taken at the same time, and (3) those in whom it produced a diuretic action in addition to that produced by water administered at the same time.

Leslie, Chicago.

Changes in the Physical Chemistry of the Blood in Patients with Anemia. I. Superficial Tension. N. Giuffré, Pediatria. **35**:301, 1927.

The superficial tension of the blood was lower than normal in twenty-two cases of anemia, including simple secondary anemia, the anemia accompanying leishmaniasis, and von Jaksch's anemia, and in one case of chloroma. Traube's method was employed in this study.

Histamine Test of Gastric Function in Children. A. Coari, Pediatria **35**:365, 1927.

Coari studied the gastric contents of infants and children before, and forty-five minutes after, the subcutaneous injection of from 0.5 to 1 cc. of histamine. She concludes as follows: 1. Histamine is ordinarily well tolerated by infants and children. 2. Its subcutaneous administration notably stimulates gastric secretion, especially hydrochloric acid, thus affording a method for the study of gastric function independent of alimentary stimulation. 3. The amount of free hydrochloric acid in infants and children is considerable. 4. In children with diseases of the gastro-intestinal tract, quantitative figures were lower than for healthy children of the same age or for children presenting conditions not referable to the gastro-intestinal tract.

Sala, New York.

Ability of the Infant's Pancreas to Digest Cell Nuclei. Einecke, Dr. Fr., Berlin, Monatschr. f. Kinderh. **35**:533, 1927.

In a previous study von Lukacz gave infants thymus which had been stained, in order to test the function of the pancreas. He then examined the stools to determine whether or not these stained nuclei were digested. The marked

excretion of these nuclei led him to conclude that the infant's pancreas has not the proper ferment.

The author reasoned that perhaps the stain prevented the digestion of the cell nuclei, and he attacked the problem in another way. He devised a diet rich in liver, one which would contain a great deal of purine. He then placed two children in metabolism frames, and by analysis of the stool and urine, determined how much of the purine entered the body. As only from 12 to 14 per cent of the purine nitrogen was found in the stool, he concluded that about 87 per cent was absorbed. His conclusions naturally differ from those of von Lukacz.

GERSTLEY, Chicago.

MECHANISM OF ANAPHYLACTIC SHOCK. G. P. SSACHAROFF, Virchows Arch. f. path. Anat. **261**:751, 1926.

In an investigation of the mechanistic theory of anaphylactic shock of Werigo, who ascribed the shock to multiple pulmonary capillary thrombi which had their origin in intravascular precipitates, the author employed five series of experiments. These consisted of the intravenous injection into rabbits of guinea-pig antirabbit precipitin serum; of the intravenous injection into rabbits consecutively of rabbit antihorse serum and normal horse serum; of the intracardiac, intraperitoneal and intrapleural injection of rabbit antiguinea-pig serum into normal guinea-pigs; of the intravenous injection into rabbits of a precipitate-containing mixture of rabbit antihorse serum and normal horse serum, and of the intravenous injection of a large dose of normal horse serum into rabbits which had been sensitized to horse serum. Only in the guinea-pigs injected with rabbit antiguinea-pig serum and in the final series of sensitized rabbits which received horse serum were any anaphylactic manifestations observed. In these the blood was fluid, the lungs were emphysematous and their blood vessels were engorged, but thrombosis was not present. The experiments did not offer any support for the view that anaphylactic shock is due to pulmonary capillary thrombosis.

O. T. SCHULTZ.

EXPERIMENTAL RESEARCHES ON THE ACTIVITY OF LIPOIDS IN PUPPIES WITH CONDITIONS RESEMBLING DYSTROPHIA. HERBERT BUSCHMANN, Ztschr. f. Kinderh. **42**:568 (Dec.) 1926.

According to Finkelstein, development of tissue is brought about by a swelling of the cells in which the factors concerned are water, salts, albumin and carbohydrate, the fixation of the process perhaps depending on fat.

A condition was produced in sixteen puppies by deficient nourishment from the eighteenth to the twenty-first day which is similar to the dystrophy and the atrophy of human infants. Without therapy, death occurred in from fourteen days to four weeks. By feeding the puppies with breast milk after previous deficient nourishment, a slow gain in weight could be obtained. With continued feeding with deficient food, a gain in weight could be obtained by parenteral lipoid therapy. This did not happen if protein bodies instead of lipoids were injected. A still greater increase in height and general condition was obtained if food with a high caloric value was given in addition to the lipoid treatment. The site of application of the lipoid activity in the body could not be determined. An explanation of this question is to be found only by a study of the chemistry of individual organs (liver ?) and of body fluids.

THE INFLUENCE OF IRRADIATED COW'S MILK ON THE OXYGEN CONSUMPTION OF ISOLATED INTESTINAL CELLS OF CALVES. H. VOLLMER and S. LEE, Ztschr. f. Kinderh. **42**:574 (Dec.) 1926.

Twelve tables are given which show that the intestinal cells of the calf, almost without exception, have a lower gaseous exchange in irradiated milk than in milk which has not been so treated. The process of radiation must alter the milk in such a manner that it thereafter lowers the primary function of the cells oxidation. This is surprising from the point of view of the antirachitic activity of irradiated milk. Since, however, ozone is known as a cell poison, the diminution of gaseous exchange in the cells may be adequately explained by the presence of ozone in the irradiated milk. These researches have shown that it is hardly conceivable that the antirachitic activation of milk by irradiation is associated with simultaneous formation of ozone.

CHOLESTERIN METABOLISM AND ITS RELATION TO THE INVOLUTION OF THE CORTEX OF THE SUPRARENALS IN INFANTS. MAX WEBER, Ztschr. f. Kinderh. **42**:633 (Dec.) 1926.

A connection cannot be demonstrated between the involution of the suprarenals and the metabolism of cholesterin. If a far-reaching occurrence, such as the degeneration of the inner layer of the cortex of the suprarenal tissue represents, has no real influence on the metabolism of cholesterin, the function of the suprarenal as the chief organ of intermediate metabolism of cholesterin is doubtful. Penetrating research is still needed of all other organs that stand in close relation to cholesterin metabolism, such as the liver, spleen and cerebrum, in order to exclude a compensatory activity of these organs, which might hide the evidence of the function of the suprarenals. Up to the present time involution of the suprarenal tissue as a result of the transition from intra-uterine to extra-uterine life represents independent developmental characteristics.

EMERSON, Boston.

METALLIC SALTS IN SERUM HORSES. H. BECKER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **47**:555, 1926.

Becker confirms Madsen's observation that the injection of manganese chloride in serum horses increases the antitoxin content of antidiphtheria serum. The results were not so favorable in the production of antitetanic serum.

PAUL R. CANNON.

INFLUENCE OF EPINEPHRINE ON TYPHOID AGGLUTININ. M. ODA, J. Pediat., Tokyo **320**:31 (Jan.) 1927.

Borchavdt found that by hypodermic injection of 1 cc. of 1:1,000 solution of epinephrine hydrochloride on the seventeenth to the ninteenth day after the intravenous injection of 1 cc. of typhoid vaccine, the formation of agglutinin is greatly accelerated; however, it loses its effect in twenty days. The author of this experiment injected epinephrine in various ways at varied intervals and tested its effect on agglutinin. He found that the effect of typhoid vaccine on the formation of agglutinin reaches its height after two weeks of injection, but that the effectiveness rapidly falls. By injecting epinephrine just before and after the time when formation of agglutinin is expected to be at its maximum, the strength of the agglutinin is somewhat increased as compared with that of control animals, but the difference is of negligible quantity. When epinephrine

was injected on the sixth, eighth, tenth and seventeenth day after the injection of typhoid vaccine, the agglutinin value rose quickly and remained high much longer than in control animals. When epinephrine was injected about one week after the injection of vaccine, the effect was thought to be most favorable.

KATO, Los Angeles.

## Nutrition

THE BACTERICIDAL PROPERTY OF COW'S MILK. F. S. JONES and RALPH B. LITTLE, J. Exper. Med. **45**:319, 1927.

The bactericidal activity of fresh raw milk from a number of cows has been tested with the nonhemolytic mastitis streptococcus. By using this organism and other means the action of agglutinin was ruled out. The milk of all cows examined inhibited the growth of the streptococcus for definite periods. The length of the inhibition period varied; the milk from some cows prevented growth for eight hours, that of others for only from four to six hours. The inhibitory action may be as strong in the milk of a young cow in its first lactation period as in that of an old cow known to be resistant to udder infection. It is possible to absorb the streptococcus inhibitory substance by first inoculating the milk with *B. bovisepticus*. It was impossible to show that the substance was increased by artificial immunization of cows with the streptococcus. Whey obtained by the action of sterile rennet solution inhibited the growth of the streptococcus to about the same extent as the milk from which it was obtained. It is inferred that the substance originates in the udder, since it differs from blood alexin in its resistance to heat, it is not increased in the whey, although the blood proteins are more concentrated, and it is not increased in the milk when the cows are artificially immunized or repeatedly exposed to natural infection.

AUTHORS' SUMMARY.

A CASE OF PROLONGED LACTATION IN AN ALGERIAN WOMAN. L. CEARD, Arch. de l'Inst. Pasteur d'Algérie **4**:93, 1926.

The article gives the analysis of the milk of a woman, about 60 years old, who was nursing her grandchild.

[ARCH. PATH.]

EXAMINATION OF GASTRIC JUICE IN CHILDREN FOLLOWING A TEST MEAL. K. IWANOFF- GLUCHOWA and A. SAWSCHINSKY, Jahrb. f. Kinderh. **61**:1 (Dec.) 1925.

A 5 or 10 per cent solution of Liebig's beef extract was used as a test meal in three children, each one having from four to six tests. The gastric juice following such a test meal is colorless after from eighty to ninety minutes, when all the extract has been absorbed into the blood stream.

The greatest secretion takes place in from one and one-half to two hours after the introduction of the extract. The juice was tested by the fractional method, using a small catheter for collection from the stomach.

THE SECRETIVE ACTIVITY OF THE STOMACH OF NURSLINGS DURING AND AFTER DIGESTION. A. B. WOLOWIK, Jahrb. f. Kinderh. **61**:9 (Dec.) 1925.

Wolowik used cabbage juice as a test meal. Several hours following the ingestion of this juice a clear gastric juice was secreted. Cabbage juice has

great power of arousing gastric secretion. During, as well as after, digestion, infants may have acid values varying from achylia to hyperacidity. Gastric secretion is usually reduced in alimentary intoxication, parenteral infection and neuropathic diseases.

THE SECRETIVE POWER OF THE FASTING STOMACH IN INFANTS. A. B. WOLOWIK, Jahrb. f. Kinderh. **61**:21 (Dec.) 1925.

Wolowik examined seventy infants and made seventy-six examinations. The gastric juice was aspirated by means of a catheter from nine to ten hours after the last meal and then every half hour thereafter for five hours. Free hydrochloric acid was present periodically in 97 per cent of normal children and absent in 28 per cent. Free hydrochloric acid was absent in 50 per cent of cases of nutritional disturbances and present in 8 per cent. Total acid varied between 2 and 60 in fractional analyses of the same gastric juice and the free hydrochloric acid between 0 and 48.

EHRMANN, Chicago.

THE PROBLEM OF VITAMINS: SECOND COMMUNICATION. FURTHER COMPARATIVE RESEARCHES ON THE HEALING OF RICKETS. WALTER SCHMITT, Ztschr. f. Kinderh. **42**:205 (Nov.) 1926.

Schmitt saw rickets develop in patients fed on a diet consistently rich in vitamins B and C; moreover, when rickets became cured with the exhibition of vitamins B and C, it happened only when the tendency to get better already existed. On the contrary, exposure to the sun's rays either worked a cure with certainty or prevented the disease even when the diet was poor in vitamins.

Comparative experiments in the feeding of three pairs of premature twins, as well as therapeutic researches on vitamin B in relation to eighteen premature infants, were entirely unconvincing as to an increased need of vitamin B in premature babies. It is not plausible that prematurity is based on a lack of vitamin B, since in countries in which beriberi exists, a tendency for women with this disease to have premature babies appears to be unknown.

During the past winter, by feeding control patients for months on the usual milk mixtures made up of milk poor at least in vitamin C, as demonstrated by experiments on animals, the author, in contrast to Reyher, was able to raise the resistance definitely or to keep it at the same level for a long time without the help of any other vitamin. No better results were obtained later in a long course of feeding with vitamin B and C, nor was the response notably increased in another series of cases in which the diet given for months was rich in vitamins B and C.

THE ANTIRACHITIC ACTIVITY OF THE WATERY EXTRACT OF COD LIVER OIL, LIKEWISE THE SIXTH COMMUNICATION ON STUDIES IN PHOTO-ACTIVITY. HERMANN VOLLMER, Ztschr. f. Kinderh. **42**:260 (Nov.) 1926.

The watery extract of cod liver oil afforded protection from rickets in a quantity of 0.1 cc. per day with the same certainty as the equivalent quantity of real cod liver oil. The extracting process did not rob the residue of its activity as vitamin, but not all watery extracts possess it.

The fraction which is active is probably not related to cholesterol, but is an unsaponified fraction of the cod liver oil. When the extract was exposed to light, this photo-activity was increased, but later it was completely lost as was the antirachitic activity.

THE CONTENT OF VITAMIN OF BONE MARROW. MARGARETE SCHÖNBERGER, Ztschr. f. Kinderh. **42**:306 (Nov.) 1926.

In spite of the beneficial effects of bone marrow, it has only a limited use in the dietary of children, since the content of antirachitic as well as of growth-producing material is small. In no case may it be thought that bone marrow can be used in place of cod liver oil or butter.

HAS THE CORRELATION OF FOODSTUFFS AN INFLUENCE ON THE LENGTH OF TIME IT REMAINS IN THE STOMACH? S. BRUCHSALER, Ztschr. f. Kinderh. **42**:381 (Nov.) 1926.

After the addition of fat to sugar solution given to healthy children, a part of the sugar solution is passed on from the stomach to the intestines, where it undergoes quick absorption. The concentration of the other part is lowered by the dilution with the secretion of the stomach. Apparently the addition of other foods is without any real influence on the time of transport of the sugar. In any case the differences found do not suffice to explain the great discrepancies which result in the glycemic reaction by the addition of fat or of fat and whey to sugar. The question of whether the duration of the stay of food in the stomach is extended by the addition of other foods to the sugar solution must be answered in the negative. It follows that the difference in speed with which a solution of food or food mixture is absorbed is not a result of anything that occurs in the stomach, but probably the result of some process in the intestine or in the liver.

EMERSON, Boston.

ON THE ISOLATION OF THE ANTIBERIBERI VITAMIN. B. C. P. JANSEN and W. F. DONATH, Mededeelingen van den Dienst der Volksgezondheid in Nederl.-Indië. **1**:190, 1927. (Tr. Roy. Acad. Amsterdam **35**:7, 1926.)

After numerous endeavors undertaken by many authors to isolate the B-vitamin and especially the antiberiberi vitamin, Jansen and Donath have succeeded in obtaining this vitamin in a crystalline form. These investigations were made in the same laboratory (at Weltevreden) in which Gryns and Eykman in 1901 made the first attempts to isolate this vitamin.

The method followed is described in detail. The raw material was the rice bran (dedek), which is cheap in India. After a treatment, which lasted for months, about 100 mg. of a crystalline substance was obtained from about 300 Kg. of dedek. After recrystallization, this substance was shown to have a melting point of 250 C. (546 F.). Part of this substance was transformed by means of gold chloride into a fine crystalline double-salt. With hydrosulphuric acid, the vitamin hydrochloride was obtained from it. The proof that these crystals were really the antiberiberi vitamin hydrochloride sought was obtained in experiments with a large number of little nun-birds, a kind of rice-birds chosen for those experiments in 1920 by Jansen. These birds were taken because when fed with washed polished rice, they develop polyneuritis within from nine to twelve days; in larger animals it usually takes longer before the polyneuritis manifests itself. It appeared, that an addition of 1½ parts of vitamin hydrochloride to 1 million parts of washed polished rice, e. g., 3 Gm. of the obtained substance each day, protected the nun-birds from polyneuritis. In men, who eat about 500 Gm. of rice daily, this quantity corresponds to 0.5 mg. of vitamin hydrochloride. On analysis, Jansen and Donath found the formula of the vitamin to be $C_6H_{10}ON_2$. Probably it contains an imidazol or a pyrimidin ring. The investigation of the formula is still going on. As

this formula is a relatively simple one the vitamin may be prepared synthetically without much expense. Provisionally the laboratory at Weltevreden has available one of the intermediary products obtained in the isolation of the vitamin, namely, an acid clay activated by absorbing vitamin from the dedek extract.

For the prevention of infantile beriberi, the investigators prepare especially an extract of this activated acid clay which can be added to the milk.

VAN CREVELD, Amsterdam.

## Prenatal Conditions

THE BACTERIAL CONTENT OF THE UTERUS AT CESAREAN SECTION. J. W. HARRIS and J. H. BROWN, Am. J. Obst. & Gynec. **13**:133, 1927.

Cultures of the contents of fifty uteri were made through the operative incision at cesarean section. The cultures were sterile in twenty-eight patients who had been in labor less than six hours. One patient not yet in labor, but with membranes ruptured for ten hours, yielded a positive culture. In the remaining cases, in which the patients were in labor over six hours, infection was found. In six of the positive cases, the membranes had not yet ruptured. Ascending infection and vaginal manipulations were considered factors in producing the uterine infection. Although premature rupture of the membranes adds materially to the danger of infecting the amniotic fluid, intact membranes did not offer an effective barrier in six cases. The relative merits of classic conservative cesarean section over low cervical section are discussed.

A. J. KOBAK.

CONGENITAL DISLOCATION OF BOTH KNEES. JACOB GROSSMAN, M. J. & Record **125**:189 (Feb. 2) 1927.

There are two forms of dislocation of the knees which should be identified separately: (1) congenital deformity due to intra-uterine pressure, which consists merely in a hyperextension of the knee rather than a true dislocation; (2) a true dislocation in which the condyles of the femur are displaced backward in their relation to the tibia. The author gives a report of a case of the latter type in an infant 1 week old. Bilateral congenital dislocation of the knees is not common. In early cases persistent manipulative treatment will give good results. Both hips in these cases should be examined as congenital dislocation of the hip may be associated.

OXYCEPHALY WITH CASE REPORT. JOSEPH H. MARCUS, M. J. & Record **125**:192 (Feb. 2) 1927.

The author states that this rare developmental abnormality embodies a type of idiocy occurring only once in 3,000 cases. He then gives the following description of the disease, taken from Feer's "Pediatrics": "A peculiar deformity of the cranium marked by the steep rise of the parietal and occipital bones with the formation of a high forehead.

"The entire head looks as though it had grown upward, while the base of the skull is often narrow. The sutures, and especially the sagittal are palpable and form a distinct ridge. The region of the greater fontanelle is often particularly prominent and almost cone shaped." He gives extracts from the cases of the disease which have been reported. In most of these cases the classical features of oxycephaly were seen: gradually progressive

impairment of vision, exophthalmos and characteristic cranial deformity. Most of the patients were below par mentally. He gives theories of its etiology and suggests surgical treatment. He next reports in detail a case of his own.

WILLIAMSON, New Orleans.

COMPLETE ABSENCE OF ONE LUNG. F. DANNHEISSER, Beitr. z. path. Anat. u. z. allg. Path. **76**:87, 1926.

The rare anomaly reported by the author occurred in a man, aged 34 years, who died as the result of a fracture of the skull. External maldevelopments were not present, and the chest was symmetrical. No vestige of the left lung could be found. The large, single, three lobed right lung extended far over to the left and covered the heart, which was situated to the left of the midline, the apex lying against the wall of the left side of the chest. The trachea was normal and divided at the usual situation into two main bronchi, both of which entered the right lung. Injection of the bronchi demonstrated the presence of two complete bronchial trees within the lung. There was only a single pulmonary artery and pulmonary vein. The various theories that have been proposed to explain the absence of a lung are briefly discussed, the author accepting a failure of development, of the *Hemmungsbildung* type, as the most probable explanation. The presence of a double bronchial tree in the single lung of his patient is accepted as evidence that the original single pulmonary anlage failed to undergo division into two lungs.

CONGENITAL ELEPHANTIASIS. H. WILLI, Beitr. z. path. Anat. u. z. allg. Pathol. **76**:98, 1926.

A male child, who died at the age of 6 days, presented a greatly enlarged right lower extremity at birth. On microscopic examination the markedly thickened subcutaneous tissue was found to contain numerous widely dilated lymphatics, many of which were cystic. Cellular proliferative reactions were not present in the surrounding tissues. The lymphatics of the brain and spinal cord were ectatic, and dilated lymphatics were present in the leptomeninges. The condition is explained as maldevelopment of the hamartoma type, which consisted in an excess development of lymphatics.

O. T. SCHULTZ.

## Diseases of the New-Born

THE PATHOGENESIS OF PEMPHIGUS NEONATORUM. FREDRICK HOWARD FALL, Am. J. Obst. & Gynec. **13**:774, 1927.

In a previous paper, the author reported isolation from pemphigus lesions of staphylococci that fulfilled all of Koch's laws. He believes that this is the usual strain of staphylococcus present in ordinary pustular skin lesions. Several cases are cited to prove the transmission from attendants or mothers to infants. He concludes that a person having an active pustular skin lesion should not be allowed in a nursery or to come in contact with linen for the nursery.

ALLEN, Chicago.

THE DIAGNOSIS OF MELENA NEONATORUM WITH ULCER OF THE ESOPHAGUS. S. DIAMANTOPOULOS, Ztschr. f. Kinderh. **42**:606 (Dec.) 1926.

A case is described which apparently shows that histologic examination would reduce the number of cases of melena considered as idiopathic. When an ulcer of the peptic type is found in melena, the genesis of the ulcer should

be discovered, if possible, for such ulcers may be related causally to diseases or birth injuries of other organs. They may be formed secondarily as a result of a disturbance of circulation.

SUBCUTANEOUS NECROSIS OF FAT TISSUE IN THE NEW-BORN: SECOND COMMUNICATION. J. BERNHEIM-KARRER, Ztschr. f. Kinderh. **42**:658 (Dec.) 1926.

Bernheim-Karrer has observed eighteen cases of scleroderma in infants, which he attributes to fat necrosis following trauma at birth, especially when fat, elderly primiparae give birth to too fat and too long babies. He has had the opportunity of examining two such babies after death. There is a difference between the fat injury due to excessive pressure and that due to mild pressure; in the one case, hemorrhages and secondary destruction of the subcutaneous fat, injury to the skin and bacterial invasion, leading to inflammation of the corium and subcutis occur; in the other case, there is little bleeding, marked edema, no injury to the skin, but a loss of staining power to sudan.

In spite of the fact that injuries to fat tissue due to excessive pressure on the one hand and mild pressure on the other do not harmonize in the microscopic picture, the same results follow clinically, for the areas of hardness form not only on the same areas of skin which were injured by the rigid soft parts of the mother or by the manipulations of the obstetrician, but also on the scrotum and the buttocks, sites of little pressure. The more frequent kind of injury is that produced by direct force; but while restitution in the epidermis and corium is completed in a few days, if no infection has occurred, the healing process of the fat tissue is slower. The chief injury is due to the cleavage of fat by the action of skin lipase, which is abetted in severe hemorrhages perhaps by serum lipase.

EMERSON, Boston.

## Acute Infections

SOME MODES OF INFECTION IN RHEUMATIC FEVER. ERNST P. BOAS and SIDNEY PINCUS SCHWARTZ, Am. Heart J. **2**:375 (April) 1927.

The authors have thought it worth while to review a series of cases in which the patients have received prolonged institutional treatment to discover what benefits, if any, may be ascribed to institutional residence. With this in view, they have studied the records of fifty-three children under 15 years of age with rheumatic heart disease, who were patients in Montefiore Hospital between May, 1921, and May, 1926.

On admission, all had organic valvular lesions resulting from previous rheumatic infection. The average stay in the hospital was two hundred and seventy-seven days, the period of institutional residence ranging from twenty-five days to three years.

Acute articular rheumatism is uncommon in children, and only two of the children of the series exhibited acute arthritis. At times fleeting pains in the joints or muscles or an evanescent pericardial rub may be the only rheumatic manifestation, or the appearance of a crop of subcutaneous nodules may offer a clue. More often the diagnosis must be made by eliminating every other possible cause of fever, and noting tachycardia disproportionate to the fever, a rise in the neutrophil count and, more particularly, the rapid appearance of a marked secondary anemia.

In a certain number of instances attacks of tonsillitis and pharyngitis, sixteen in all, were related to rheumatic infection.

Some of the observations suggest a close relationship between certain instances of pulmonary infection and rheumatic fever.

The tonsil does not seem to be so important a portal of entry for rheumatic infection as is generally supposed, and tonsillectomy appears to be of little avail in reducing the hazards of reinfection.

The authors were almost compelled to come to the conclusion that febrile attacks, which occurred in three quarters of the series, are due to contact infection; in fact, there is much evidence in the literature supporting the view that rheumatic fever may partake of the nature of an epidemic disease and that contact infection is possible. A number of local epidemics have been described. In 1887, Feltkamp described infection in a ward similar to those the authors have observed. During the World War, Grenet noted that rheumatic fever was confined to certain regiments.

In adults, reinfection is infrequent, and the duration of each attack of arthritis or carditis is usually a few weeks; in children reinfection is the rule, and attacks lasting several months are not uncommon.

The most hopeful suggestion in the present state of our knowledge, first proposed by Raven and echoed by Swift and others, is to provide sanatorium treatment for rheumatic subjects, analogous to that established for tuberculous patients. Patients harboring rheumatic infection would be treated for periods of from six to twelve months or longer under a strict sanatorium regimen, with the employment of all of the usual aids of rest, proper food, light and air, with a closely supervised resumption of the full activities of health.

MANNING, Santa Barbara, Calif.

THE NERVOUS COMPLICATIONS OF VARIOLA, VACCINIA AND VARICELLA WITH REPORT OF CASES. R. E. WILSON and F. R. FORD, Bull. Johns Hopkins Hosp. **40**:337 (June) 1927.

There is a valuable review of the literature on these conditions.

Four cases of vaccinia encephalomyelitis are reported, with two autopsies. Recovery in two cases was complete, except for slight residual spasticity of the legs. Autopsy in one case showed a diffuse nonsuppurative inflammatory process in all parts of the central nervous system, most severe in the pons and midbrain and least severe in the cortex and thoracic cord. The histologic picture is different from that seen in epidemic encephalitis.

The authors report three cases of involvement of the central nervous system in varicella. This brings the total of published case reports to twelve. Symptoms developed between the fourth and fifteenth day of the disease. They were ophthalmoplegias, nystagmus, vertigo, vomiting, tremor, choreiform movements, spastic weakness of the legs and sphincter disturbances. Sensory loss was unusual. There were no deaths, and recovery was nearly complete in every case.

The authors think that the condition is less uncommon than has been believed.

LYTTLE, New York.

SEPARATION OF VIRULENT CULTURES OF B. DIPHTHERIAE INTO VIRULENT AND AVIRULENT TYPES. MARY L. COWAN, Brit. J. Exper. Path. **8**:6, 1927.

The author succeeded in separating an avirulent, nontoxicogenic type ("R") from a virulent culture of *B. diphtheriae*.

ARCH. PATH.

RÔLE OF RETICULO-ENDOTHELIAL SYSTEM OF THE CUTIS IN EXPERIMENTAL VACCINIA AND OTHER INFECTIONS: EXPERIMENTS WITH INDIA INK. J. C. G. LEDINGHAM, Brit. J. Exper. Path. **8**:12, 1927.

Infiltration of an area of the skin with ink and subsequent vaccination suspends all response by the naked eye. Infiltration with, say *Streptococcus erysipelatis* may have the same effect. It is suggested that local defense is increased by stimulation of the reticulo-endothelial cells to proliferate.

ARCH. PATH.

THE EFFECT OF DIPHTHERIA TOXIN ON BLOOD SUGAR AND INSULIN ACTION IN RABBITS. R. D. LAWRENCE and O. B. BUCKLEY, Brit. J. Exper. Path. **8**:58, 1927.

It is shown that in rabbits diphtheria toxin in some way leads to reduction or suspension of the action of insulin. This effect is ascribed to the stimulation by the toxin of the thyroid and suprarenal, which have an antagonistic influence on insulin.

GLANDULAR FEVER IN CHILDREN. JAMES BURNET, Edinburgh M. J. **34**:89 (Feb.) 1927.

Burnet contributes a short article with six illustrative case reports. The cause of the disease is not known, but may be associated with nasopharyngeal infections, atypical cases of scarlet fever or German measles. About all that can be said is that it is an acute infectious febrile disease involving usually the posterior cervical glands, and in some cases the other lymphatic glands and the spleen, with no tendency to suppuration, but with a transient rash in certain instances. The author did not confirm the existence of a mononucleosis, which has been ascribed to this disease. He makes no attempt to prove that glandular fever is a primary entity.

THE SERO-PROPHYLAXIS OF MEASLES. W. T. BENSON, Edinburgh M. J. **34**:216 (April) 1927.

After reviewing the literature, Benson reports the results obtained in the City Hospital of Edinburgh from the passive immunization of hospital children exposed to outbreaks of measles in the ward. The disposition of the beds occupied by susceptible infants is shown by diagrams. Twelve such children remaining in the exposed wards were given convalescent serum, in a dose of 10 cc. for those under 5 years of age, and 15 cc. for those over that age. Only one child developed measles, and this was of a mild abortive character. Those protected got the serum on or before the fourth day after exposure.

Benson believes the method of great value, especially in hospital practice, and that immune serum in from 15 to 30 cc. may well be used when convalescent serum is not obtainable.

NEFF, Kansas City.

ON IMMUNIZATION AGAINST CERTAIN INFECTIOUS DISEASES. S. MONCKTON COPEMAN, Proc. Roy. Soc. Med. **20**:43 (Nov. 1) 1926.

After the work of immunization against diphtheria was carried out at the Bristol Infirmary, this disease has been a much less frequent source of trouble. In the annual report of the Metropolitan Asylums' Board for last year, reference was made to the increasing prevalence of diphtheria in London. Diphtheria is certainly the most destructive of any of the infectious diseases encountered in

Great Britain; in London at any rate, it appears to be resisting attack. The time has come for the adoption of measures calculated to restrict the depredations of the disease more effectively than hitherto.

To this end the suggestion was made that authorities on education should follow the lead of New York and undertake the testing and immunization by the Schick method of all children of school age. The author further suggested that all children of preschool age should also be immunized. As a high percentage of infants over the age of 6 months are susceptible, considerable saving of time and energy can be gained by omission of the Schick test. Research is being directed to the possibility of reducing the three immunizing doses now required to two or even one. Reduction in the number of inoculations requisite for protection would undoubtedly constitute a valuable advance toward a more general acceptance of the method on the part of parents. The immunization of all nurses employed in fever hospitals should be carried out. This has been the rule at the Bristol City Hospital since January, 1922, with the result that not one member of the staff has ever developed clinical diphtheria.

The work done by the Dicks of Chicago on immunization in connection with scarlet fever is then described. Research has been continued up to the present time by the medical officers' Committee on Scarlet Fever, which was appointed by the Ministry of Health and in due course will receive official publication. In the case of measles the method of immunization by convalescent serum was first employed by Nicolle and Conseil and has subsequently been employed by Park and Zerengher and by Richardson and Conner in America. The original methods have since been modified and production of active immunity has been attempted with some measure of success. The methods of achieving passive immunity are then described.

STRIAE PATELLARIS FOLLOWING TYPHOID FEVER. J. D. ROLLESTON, Proc. Roy. Soc. Med. **20**:319 (Feb.) 1927.

The case reported was in a girl, aged 14 years. The striae patellares were noted on the forty-third day of the disease. They consisted of symmetrical purplish transverse stripes on the skin about 1½ inches (12 cm.) above the upper border of each patella, and they measured from 1 to 1¾ inches (2.5 to 4.3 cm.) in length. There was one on the left and three on the right. The skin was otherwise normal. This condition has received various names: striae atrophicae, striae cutis distensae, striae albicantes, "Vergetures" of the French and "falsche narben" of the Germans. It is encountered after many infectious diseases but is commonest after typhoid. A brief summary is given of the literature on this condition.

WILLIAMSON, New Orleans.

EXPERIMENTAL RESEARCH ON SCARLET FEVER. CHARLES NICOLLE, E. CONSEIL and P. DURAND, Arch. d. Inst. Pasteur de l'Afrique du Nord **15**:229, 1926.

With a hemolytic streptococcus isolated from the tonsils of a scarlet fever patient, an identical infection was reproduced by tonsillar inoculation in a sensitive normal subject. A reaction was produced in other sensitive persons with the filtered and nonfiltered urine of the same patient, the inoculations being intradermal and subcutaneous.

G. B. RHODES.

INTRADERMAL VACCINATION IN PERTUSSIS. V. NALLI, Pediatria. **35**:225, 1927.

The author has used intradermal vaccination for the treatment and prevention of pertussis. The mixture employed is a 25 per cent solution of stock

vaccine in a hypertonic 80 per cent solution of saccharose, the latter rendered slightly irritating by the addition of a small dose of calcium chloride (the amount of the last ingredient is not specified). By thus inducing a local inflammatory reaction, he retards the absorption of the vaccine and prolongs the local production of immune bodies. Good results are claimed, the author asserting that usually after one vaccination, always after two, the character of the disease is modified from a serious condition to an ordinary mild infection of the upper part of the respiratory tract, which is easily amenable to medical treatment. Although a detailed statistical report is not given, Nalli seems to have had the opportunity to study and to treat many patients. One looks forward to a more detailed report of the technic and results of this treatment, which he asserts is superior to all others, including the notoriously unreliable subcutaneous administration of vaccine.

PNEUMOCOCCIC PERITONITIS IN CHILDREN. M. BERGAMINI, Pediatria. **35**:401, 1927.

Four interesting cases of this condition are described in detail, in all of which the patients were operated on and cured. In all cases, the process was found well localized in the lower part of the abdomen. In the first patient, a dead worm 11 cm. long (*Ascaris lumbricoides*) was found at the bottom of the pus sac in the right iliac fossa, but rupture of the intestine was not actually demonstrated at operation. Two of the cases developed slowly. In the first case, fully eight months elapsed between the onset and the operation which was performed when the child was brought to the hospital, after the sudden discharge of yellowish, foul pus from the umbilicus. The condition in the other slowly developing case had been diagnosed as tuberculous peritonitis, and the true nature of the malady was revealed by the spontaneous establishment of a sinus at the umbilicus. The second child had had abdominal colicky pains for months and months.

The other two patients came to operation within three weeks of the onset.

The chief diagnostic points are: age of the child (school age), pyrexia, herpes labialis, tendency to lower abdominal localization with little production of fluid, abdominal enlargement with umbilical protrusion and hippocratic facies. In the acute cases one must differentiate acute appendicitis, streptococcic peritonitis and perforation; in the slowly developing cases, tuberculous peritonitis and the typhoid and paratyphoid states must be differentiated.

PRIMARY PNEUMOCOCCIC PERITONITIS. B. VASILE, Pediatria. **35**:488, 1927.

A girl, aged 5, had been seized with fever, vomiting and profuse diarrhea on June 19, 1926, one month prior to admission. Two days later, there was severe abdominal pain; the vomiting had ceased; the diarrhea gradually subsided, and ceased in a few days. The fever persisted and gradually began to be remittent in character. The abdominal pain slowly ceased, but tenderness persisted. Three days before admission, there was a protrusion of the umbilicus, which was red and tender. There had been a gradual, steady loss of weight.

On examination, the abdomen was found to be moderately distended, with prominence of the hypogastrium. There was resistance over both lower quadrants, more marked between the pubis and umbilicus, where there was also marked tenderness. The liver and spleen were not enlarged.

Three days after admission, the child evacuated, in the stool, abundant quantities of greenish-yellow pus, which contained gram-positive, lancet-shaped,

encapsulated diplococci. This was followed on the following day by a disappearance of the periumbilical swelling. Two days later, pus did not appear in the stool, the fever began to rise, and abdominal distention returned. Four days after this, a sinus appeared at the umbilicus, from which foul greenish-yellow pus was discharged; from this the pneumococcus was isolated in pure culture. Four days later, the child was taken home improved, and still enjoys good health.

SALA, New York.

AN EPIDEMIC OF FIFTH DISEASE (INFECTIOUS ERYTHEMA). G. TACCONE DOTT, Riv. di clin. pediat. **25**:145, 1927.

An epidemic of fifteen cases of infectious erythema occurred in a school in Milan. The only symptom was the erythema. A white blood count was made in six cases; in one it was 13,200, and in the others between 4,400 and 7,500. No organisms were found on culture, either anaerobically or aerobically.

HIGGINS, Cincinnati.

INFLUENCE OF TUBERCULIN ON THE PAROXYSMAL STAGE OF PERTUSSIS. C. STUHL, Arch. f. Kinderhk. **75**:4 (March) 1925.

Seventeen children with pertussis were given injections of Koch's old tuberculin, starting with 0.0001 mg. and repeating every three or four days in gradually increasing dosage. Graphs are shown to illustrate the beneficial effects on the number of paroxysms.

T. C. HEMPLEMANN.

GONORRHEAL ARTHRITIS IN INFANTS. M. GUNSBERG, Berlin, Monatschr. f. Kinderh. **35**:486, 1927.

The author reports three cases of gonorrheal arthritis in infants, with involvement of many joints. In two of them, the course was so severe as to be typical of a sepsis. In one of these the child died.

The involvement of the joints was characterized by the rapid development of edema, by rednes and by seropurulent effusion into the joint. Cultures taken from the joint cavities were sterile. The process was accompanied by high, usually remittent, fever and exacerbations coincidental with the involvement of new joints. In the severest cases, gonorrheal abscesses formed in the tissues. Death in the author's series and in those of other observers, occurred from intercurrent infection.

The diagnosis is relatively simple. The picture may be confused with the involvement of many joints in congenital syphilis.

In a number of these children the source of the infection was not clear. There was no evidence of gonorrheal involvement other than in the joints. The supposition is that the infection was congenital.

Treatment is aided by the tendency to spontaneous recovery. Rest is the most important factor. In these three cases, the author used a stock gonococcus vaccine. He believed it was of value.

PROPHYLACTIC USE OF SCARLET FEVER SERUM (BEHRING). HEDWIG MULLER, Berlin, Monatschr. f. Kinderh. **35**:514, 1927.

The author tried the Dick serum in prophylactic doses but was not satisfied with the results; this serum was prepared by the Behring concern. Immunity did not seem to be well established and did not last over two weeks.

GERSTLEY, Chicago.

DIPHTHERIA IMMUNIZATION BY TOXOID. ST. PROGULSKI and F. FEDLICH, Wien. klin. Wchnschr. **40**:284 (March 3) 1927.

Following reports of deaths in a Vienna infant asylum from use of toxin-antitoxin for prophylaxis against diphtheria, the authors turned their attention to toxoid (anatoxin) as a safer substitute method. The toxoid was prepared from toxin by addition of formalin and prolonged application of heat. Using Ramon's method, which requires five weeks to complete, the authors obtained negative Schick reactions from four to eight weeks later in 102 of 121 children in an orphanage. They later investigated Krause's preparation, injecting three doses subcutaneously at three day intervals in amounts of 0.1 cc. of toxoid in 2 cc. of physiologic sodium chloride solution. Eleven of thirteen patients were rendered negative to the Schick test at the end of forty days. No general symptoms followed the injections. They recommend this method, especially in epidemics, because it requires only eight days to complete.

VALUE OF DICK TEST. O. TEZNER and G. UNGAR, Wien. klin. Wchnschr. **40**:616 (May 12) 1927.

Since there have been conflicting reports from European observers as to the specificity and clinical value of the Dick test, Tezner and Ungar investigated these points. They were of the opinion that the specificity of the test had been adequately demonstrated and considered rather that false positive and negative reactions were due to extrinsic factors which altered the reactivity of the skin.

Moro's observation, that vaccine can change the reaction of a person to a tuberculin test, led the authors to investigate the effect of smallpox revaccination on the Dick test. Four patients having positive Dick tests showed no change after revaccination. Four out of five persons with negative tests were found to be positive approximately three weeks after revaccination. These included two patients convalescing from scarlatina. Two children giving positive Dick reactions gave negative reactions after the administration of nirvanol to the point of producing an exanthema. A third child, in whom the drug caused no rash, continued to have a positive reaction. Using as donor one of the children made negative to the Dick reaction by nirvanol, blood transfusion of an anemic, rachitic infant converted its reaction to the Dick test from negative to positive.

The authors conclude from their experiments that the Dick test is specific but that its outcome may be altered by variations in the sensitivity of the skin. They do not believe that the test should be abandoned clinically but recommend that further investigations be made to determine the modifying factors.

OLMSTED, Seattle.

THE DIAGNOSIS OF PNEUMOCOCCIC PERITONITIS. JOSEF K. FRIEDJUNG, Ztschr. f. Kinderh. **42**:523 (Dec.) 1926.

It has always been a question as to when there should be surgical intervention in cases of pneumococcic peritonitis. In most cases, this disease is recognizable in the acute stage by fever, sudden abdominal pain, vomiting, diarrhea, high pulse rate, cyanosis of the lips and no apparent resistance; all these symptoms occur almost always in girls from 2 to 14 years of age. Friedjung says that the time for intervention is during the second stage, that of abscess formation, when the general condition has become sufficiently improved. In many cases convalescence follows the breaking through of the abscess or reabsorption of the exudate, and intervention is not necessary.

THE DICK REACTION AS A PROOF OF IMMUNITY TO SCARLET FEVER. FIFTH COMMUNICATION. E. NOBEL and F. SCHÖNBAUER, Ztschr. f. Kinderh. **42**:622 (Dec.) 1926.

The authors state that for the purpose of immunization only small doses of the toxin should be used, as great quantities of toxin, that is, about 3,000 skin doses, may produce severe collapse and are not without risk. In their opinion, the duration of immunity, that is, the continuation of the negative Dick test after injection with Dick toxin, does not stand in direct relation to the quantity of toxin used. In the majority of cases, a negative Dick test after immunization will become positive in about ten months. A negative Dick test after injection of Dick toxin is not, on the whole, evidence of true immunity to scarlet fever.

RELAPSING FEVER IN CHILDREN. G. S. LEVY, Ztschr. f. Kinderh. **42**:627 (Dec.) 1926.

From 1917 to 1924, 360 cases of relapsing fever were observed in the author's clinic in Odessa, and among them were many cases complicated with typhus fever; one patient had not only these two diseases, but typhoid fever as well. The rise of temperature after a short period of apyrexia, from two to four days, means a complication of relapsing fever by another disease, for normally the duration of the first period of apyrexia does not last less than a week. If relapsing fever occurs with typhus fever, an exanthem is generally lacking. Cases in which relapsing fever and typhus occurred together ran a course without any other complication. A leukocytosis before the crisis in relapsing fever generally indicates another paroxysm, and a normal count of leukocytes or a diminution indicates that there will not be another paroxysm. Insufficient food for the mother favors the more frequent appearance of relapsing fever in the infant. Change in immunity by hunger may cause an increase in the number of cases and an atypical character of the apyrexia.

EMERSON, Boston.

## Chronic Infections

STUDIES IN TUBERCULOSIS: VII. THE IDENTIFICATION OF A SKIN-REACTING SUBSTANCE IN TUBERCULOUS SERA. FREDERICK EBERSON, Am. Rev. Tuberc. **15**:127, 1927.

A heat-sensitive, skin-reacting substance of the nature of a toxin has been identified in the blood serum of tuberculous patients and guinea-pigs. It is not found in normal human or guinea-pig serum. The substance does not behave like tuberculin or its related elements, which are heat-resistant, and it exists independently of them. It is present in largest amounts in advanced tuberculous infections with profound toxemia, and is apparently destroyed by heating at from 60 to 65 C. for from twenty to forty-five minutes. In normal animals, this unheated substance gives a positive skin test, owing to its interaction with normal antibodies for tubercle products. The method devised for identifying this specific skin-reacting substance depends, in principle, on a living "indicator," the guinea-pig, which measures related or identical elements in the serum to be tested. The procedure was made possible by a previous demonstration that normal animals could be sensitized with fractional tuberculins prepared from nonprotein substrates. Skin reactions, obtained according to the technic described in these experiments, are referable to an addition or subtraction of one or more of the interacting substances present

in tuberculous serum and in the tissues of the experimental animal. Evidence is adduced to show that the heat-labile substance, probably a toxin, in tuberculous serum, can be used as a measure of the circulating antibodies in both normal and tuberculous persons. A test of this type may serve as an index of the bodily resistance to tuberculous infection in both groups. Certain theories and hypotheses regarding tuberculin and skin sensitiveness in tuberculous and normal persons and in animals find an interpretation based on controllable experimental evidence. An explanation is offered for negative tests in advanced tuberculosis, and, furthermore, positive reactions with tuberculous serums in apparently normal persons are attributed to a toxin. Accordingly, the results with the autoserum test of Lenz and with modified autoserum and the Wildbolz reactions take on a somewhat different aspect.

H. J. Corper.

Bismuth Thioglycollate in Experimental and Clinical Treatment of Syphilis. O. M. Gruhzit, Edward Lyons and Ralph Perkins, Arch. Dermat. & Syph. **15**:550 (May) 1927.

This preparation of bismuth is said to have numerous advantages over the tartrates. It is water soluble and remains so after intramuscular injection. It causes only slight necrosis as compared to the tartrates and is absorbed in less than two hours. No lumps are produced, and there is no danger of cumulative effects. It produces no demonstrable visceral damage in therapeutic dosage. With its use syphilitic lesions heal readily, and the Wassermann reaction is influenced rapidly and permanently. It is stated to be from one half to one third as toxic as the tartrates and twice as efficient. The optimum dose is from 2 to 2.5 mg. per kilogram repeated three times a week.

Syphilis to the Third Generation. C. P. Bondurant, Arch. Dermat. & Syph. **15**:695 (June) 1927.

Two family histories are given in which it is thought that syphilis was transmitted to the third generation. Incidentally a case is reported of a woman, aged 35, with parenchymatous keratitis dependent on an inherited infection.

Jeans, Iowa City.

Early Tuberculosis of the Mesentery Lymph-Nodes. Fritz B. Talbot, M. Clin. N. Amer. **10**:1173 (March) 1927.

The existence of this condition may be suspected if a child has persistent symptoms of indigestion without demonstrable cause, and does not respond as he should to dietetic treatment. Diagnosis depends mainly on the presence of recurrent attacks of pain, protuberent abdomen, and a low persistent temperature in an irritable, undernourished child. Final diagnosis is made by the demonstration of pathologic changes in the glands by the roentgen ray, a positive tuberculin cutaneous test or the isolation of tubercle bacilli from the stool. Clay-colored, "soap" stools, so often found in this condition, are due to interference with the absorption of fat as a result of blocking of the lymphatics. If the diet contains a large amount of fat in an endeavor to make the child gain weight, a secondary indigestion may result and may intensify the symptoms. Heliotherapy is the most valuable curative measure, and under its use, in the majority of cases, there is continuous and progressive improvement.

It is of great importance to recognize and diagnose cases of this type at an early date before the glands break down and the disease becomes so generalized that it cannot be controlled by any method of treatment.

SMITH, Ogden, Utah.

THE PREVENTION OF DIPHTHERIA. J. GRAHAM FORBES, Medical Research Council, Special Report Series No. 115, 1927.

With the introduction of the active use of antitoxin in 1894, a radical change occurred in the treatment for diphtheria. An equally great advance has taken place in its prophylaxis since the advent of the Schick test and the active immunization of human beings with toxin antitoxin. Active immunization has been carried on in a rather broad way in New York City and other cities of the United States for about ten years, but not until the last four to six years has much been done in England. In London the rate of incidence surpasses, and the death rate nearly so, that of any other city in Great Britain or almost any large city of the world.

Naturally, most of the work has been done in children between the ages of 2 and 15 years. Children 5 years old and under receive active immunization treatment, and from three to six months later they are given the Schick test. If the reaction is positive, the treatment is repeated until the test is negative. In children over 5, only those showing a positive Schick test are treated, the test being repeated in from three to six months after treatment and treatment repeated if necessary.

Since its inauguration five years ago in London, as well as in other cities of Great Britain, it has proved to be of great economic importance in the saving of work for the health department, to say nothing of the much more valuable factors of lowered morbidity and mortality.

In Great Britain, protection for the general population is carried on mainly through welfare clinics, county and municipal schools, residential schools, homes, orphanages and contagious disease hospitals. The immunization rate in Scotland is seventeen times greater than that in England and Wales. In New York City the diphtheria death rate has dropped from 22.7 per one hundred thousand in 1918, to 7.9 in 1926.

BARNETT, Chicago.

CONGENITAL SYPHILIS. JAY FRANK SCHAMBERG, Tr. Coll. Phys. Phila., 1926, page 126.

In the specific treatment of congenital syphilis, Dr. Schamberg claims good results from the use of weekly injections of potassium tartrobismuthate in addition to injections of arsphenamine. He also emphasizes the value of building up bodily resistance by general hygienic measures.

LESLIE, Chicago.

ACTINOMYCOSIS IN A GIRL OF TWELVE YEARS. F. E. JARDINE, Edinburgh M. J. **34**:52 (March) 1927.

A child was shown who, one year before, had suffered a contusion of the chest wall without abrasion. This girl had never been in the country, near cattle, nor had she ever eaten grain or straw. During the year following the trauma, she had lost weight, and had been admitted to several hospitals for examination. She had pain in the chest, and dulness in the lower part of the right lung. At paracentesis no fluid was found, but an abscess developed

later at the site of puncture. Expectoration did not occur until eight months after the onset of the symptoms, but from the *Streptothrix* was obtained. The disease and the roentgenogram gave the appearance of miliary tuberculosis. At this time gross extension of the lesions occurred over the entire wall of the chest. From the affected areas pus and sago grains were discharged. The roentgenogram showed lesions on the surface of one lung and the consolidation of the lower lobe of the opposite lung. The blood showed a secondary anemia, polymorphonucleosis of 84 per cent, but no eosinophilia. The general picture was typical of actinomycosis. Treatment with massive doses of potassium iodide has been without effect, and roentgen-ray treatment may be tried.

TREATMENT OF TUBERCULOSIS BY SANOCRYSIN. SIR ROBERT PHILIP, Edinburgh M. J. **34**:121 (March) 1927.

This communication deals with adults treated by "Sanocrysin" with somewhat favorable results. The author believes that proposed remedies for tuberculosis should be tried in children, as it is in early life that the earliest expressions of tuberculosis are found. He concludes with a brief statement that he has recently watched the effect of "Sanocrysin" on tuberculous children, and has been disappointed with the intramuscular introduction of this remedy, which causes local pain and other untoward symptoms.

TUBERCULOUS LESIONS IN INFANTS. CHARLES MCNEIL, Edinburgh M. J. **34**:133 (March) 1927.

During an exhibition of patients and specimens, McNeil showed some large, thin sections of the entire lung, illustrating tuberculous lesions in infants. In an infant, aged 15 months, dying of progressive wasting and weakness, the section of the right lung showed the root filled with a mass of tuberculous glands, the process invading the adjacent lung by spread along lymphatic paths. The terminal bronchopneumonia was recent and nontuberculous. The opposite lung had widely scattered lymphatic tuberculosis.

In an infant, aged 11 months, with cough, low fever and wasting for four months, there was a cavity in the right apex, lymphatic tubercles in clusters in the lower lobe, and caseous root glands. The opposite lung showed lymphatic spread of tubercles.

An infant, aged 5 months, sick fourteen days, had uncountable tubercles throughout both lungs, more massive at the bases. The spread was pneumonic through the alveoli, but there were older processes in the lymphatic system.

McNeil reports also an extensive bronchopneumonia in a child, aged 1 year, with tubercle bacilli in the sputum, a positive Pirquet test, but with gradual and complete recovery.

NEFF, Kansas City.

THE THYROID IN TUBERCULOSIS OF CHILDREN. REMO DARDANI DOTT, Riv. di clin. pediat. **25**:163, 1927.

The thyroid gland in children, as in adults, seems especially refractory to tuberculous infection. In only one of one hundred autopsies on children with tuberculosis (sixty of which were cases of miliary tuberculosis) was there macroscopic evidence of tuberculous granuloma or of miliary tubercles. Of seventeen glands studied microscopically, only four showed miliary tubercles, which, however, were scattered. Other microscopic observations on the thyroid were inconstant, with the exception of the increase in connective tissue which was present in fifteen of the seventeen cases.

HIGGINS, Cincinnati.

THE PROGNOSIS OF SCROFULA. F. KRUSE, Ztschr. f. Kinderh. **42**:505 (Dec.) 1926.

It has frequently been observed that scrofula is healed without leaving demonstrable traces of severe injury to the organism in general, that it does not lead to tuberculosis and that it might even be looked on as defensive. According to the author, a typical form of secondary tuberculosis is present in scrofula in children with high grade allergy, which prognostically does not run a more favorable course than the active tuberculosis of childhood in general. The prognosis is relatively good. Statistics show that pulmonary tuberculosis in cases of scrofula is not so rare as has often been assumed. The author observed a series of cases of severe internal tuberculosis in which the patients had had scrofula earlier; eight severe open pulmonary cases, three earlier open, now closed, two extensive closed pulmonary cases, one severe case of adhesive peritoneal tuberculosis with high fever, one solitary tubercle of the brain; and further, two severe cases of open pulmonary tuberculosis in which swellings of isolated cervical glands had occurred. In eleven out of eighty children with open pulmonary tuberculosis, in about 14 per cent, there was a history of scrofula in which the isolated cervical glands had not been considered scrofulous.

THE PROGNOSIS OF SCROFULA. E. NOBEL, Ztschr. f. Kinderh. **42**:521 (Dec.) 1926.

As Kruse discused the question of how many children with scrofula had pulmonary tuberculosis in later life, Nobel makes a few comments on the question of how many patients with pulmonary tuberculosis have had symptoms of scrofula. Of twenty-three cases, twenty patients were examined from eight to twelve years after the onset of scrofula, and no serious lung complication or extension of tuberculosis was found, while three apparently died of tuberculosis. In only 15 per cent of the cases of scrofula had a bad prognosis been given. Nobel did not make a comparison between the progress of scrofula and of other types of tuberculosis; he merely tried to determine in what way scrofula increases the tendency to an extension of tuberculosis. Eighty-five per cent of the patients with scrofula recovered and did not have further tuberculosis.

OUTPATIENT TREATMENT OF CONGENITAL SYPHILIS. J. CASSEL, Ztschr. f. Kinderh. **42**:541 (Dec.) 1926.

One hundred thirty-four new-born babies and infants with congenital syphilis, most of them of legitimate birth, came under Cassel's observation during the seven and one-half years between 1916 and 1924. Among those who received treatment, the mortality was only 13 per cent. With all the disadvantages of outpatient treatment, especially of infants at the age at which some of these patients were accepted, such a low figure speaks well for what can be done if Cassel's dictum is carried out, namely, that systematic, not symptomatic, treatment should be used. While a lasting negative Wassermann reaction is not held as the sole proof of cure, it is about the best that can be hoped for outside of the wards, where, in addition to other advantages, lumbar punctures are so much more easily made. Ophthalmoscopic examinations, however, help to overcome this deficiency to a great extent. Sixty-eight per cent of nineteen untreated patients, showed pathologic eyegrounds, while only 7 per cent of treated patients showed alterations. The first course of treatment, four being given usually, is the one of great importance, and the author

believes that single treatments must be longer and better than they have been up to the present time, and that observation and treatment must extend over a longer time. He discusses the results of his treatment under two headings: (1) length and weight and (2) intelligence and character.

Of twenty-one children who had been systematically treated from the beginning, the majority showed an increase in length over the normal but the reverse as to weight. It could not be said of fourteen children who had received treatment satisfactory, except that it had been started late in infancy, that under the influence of this chronic infection they were hypotrophic. The cases are too few, and there are so many factors besides the chronic infection that a general law cannot be drawn.

If the children are fidgety, stubborn, quarrelsome, restless in their sleep, have increased reflexes and show inadequate powers of endurance in play, and work, they are considered neuropathic. There is, without doubt, a close relation between congenital syphilis and neuropathy, since a majority of the parents are found to have suffered likewise, and since in any number of nonsyphilitic children of the same station in society such a high percentage of neuropaths is never found.

Observation over a series of years, therefore, does not show an unfavorable bodily and mental development, but the children are still too young to determine what their character will ultimately be. Nevertheless, the attempt to follow cases for years is worth while, and it can be done only in the outpatient department. It could not have been accomplished at all in the cases studied if the cost of obligatory treatment had not been borne by the city of Berlin.

EMERSON, Boston.

EFFECT OF BISMUTH ON CONGENITAL SYPHILIS. KIKUO NAGAMINE, J. Pediat. (Tokyo) **320**:44 (Jan.) 1927.

The author used a preparation which contains iodine and quinine, together with 0.03 Gm. of metallic bismuth for each cubic centimeter. By intramuscular injection of this preparation in twenty-eight cases of congenital syphilis, he found that it was effective in curing such symptoms as condyloma, infiltration, alopecia, snuffles, pseudoparalysis and rhagades, but the effect was weak as compared with that of arsphenamine. This drug is best given to atrophic infants, as nutrition is favorably influenced by it. The serologic test was also favorably influenced, as it became negative in many cases after one course of treatment which consisted of fifteen injections twice weekly. There was no local reaction at the site of injection. The kidney disturbance was seen in two cases, but after treatment the patient quickly recovered. The urine must be tested constantly. A slight elevation of temperature was seen after injection, but there were no other ill effects.

KATO, Los Angeles.

## Internal Diseases

ACUTE STAPHYLOCOCCUS AUREUS ENDOCARDITIS. LOUIS M. WARFIELD, Am. Heart J. **2**:576 (June) 1927.

Dr. Warfield reports a case of a well-built unmarried girl, aged 17, who had suddenly gone into convulsive seizures. She had never been ill before. Four or five days previously, she was in her usual good health except for a slight cold. Two days before death, she complained of headache and backache but was up and about as usual. She came home on the afternoon of the next

day apparently in her usual good health and remarked that she was tired and thought she would go to bed early. The next day she was taken with a convulsion. From that time on she passed from one convulsion into another, never becoming conscious between the convulsions. There were positive Babinski, Gordon and Oppenheim reflexes, and ankle clonus and increased knee reflexes were present. A tentative diagnosis of meningitis was made. A spinal puncture was done; the fluid was clear and contained 20 cells to the cubic millimeter. The final diagnosis was acute epidemic encephalitis.

At autopsy the pericardial sac contained about 100 cc. of clear yellow fluid. The heart was of normal size, and scattered over the surface were numerous petechial hemorrhages with pale centers. When the heart was opened, similar hemorrhages were seen through the endocardium and also in cut section of the muscle. Both the mitral and tricuspid valve, leaflets were thickened, producing considerable stenosis of both orifices, especially the mitral. There was slight thickening of both the pulmonary and aortic cusps. Superimposed on the thickened mitral valve was a dark-colored, only slightly raised, recent, small warty vegetation extending along the valve for about 1 cm., and extending down on the chordae tendinae of the anterior leaflet. From direct smears of the vegetation on the mitral valve, gram-positive cocci were found. Cultures made from this spot from the heart's blood and spleen all showed pure growth of *Staphylococcus aureus.*

Petechial hemorrhages which show pale centers are said by Libman to be characteristic of infection with *Streptococcus viridans.* Here was an infection with *Staphylococcus aureus* producing a pathologic picture similar to that produced by *Staphylococcus viridans.*

MANNING, Santa Barbara, Calif.

LEUKEMIA — A SARCOMA: BONE EVIDENCE. REPORT OF TWO CASES. S. M. CONE, Arch. Surg. **14**:542, 1927.

Many authorities have recognized the similarity between leukemia and tumors, and leukemia has been looked on as a tumor in a fluid medium. Leukemic infiltration of fixed tissue is well known, and its malignant characteristics are recognized. The author feels that the difference between some cases of myeloma with metastases and leukemia is one of consistency rather than a fundamental difference in cell type. To support his opinion, he describes two cases of leukemia in which invasion of brain, liver, intestine, spleen, serous membranes and bone occurred. There was definite invasion of bone by a specific cell of the myelocyte series, which caused bone absorption and also filled the bone marrow.

N. ENZER.

NEUROBLASTOMA OF THE ADRENAL GLAND (HUTCHINSON TYPE). REPORT OF A CASE. MAX LEDERER, J. Cancer Research **10**:377, 1926.

Lederer reports a case of a neuroblastoma of the left suprarenal gland found at necropsy in a girl, aged 4½ years. Clinically, the case was characteristic of this variety of tumors in that it showed a left proptosis roentgenographic evidences of malignancy in the cranium, and a mass in the left hypochondriac region. From a pathologic standpoint, the growth displayed its usual features. It originated in the medullary part of the suprarenal gland. Although nerve fibers could not be demonstrated in the sections, numerous ganglion cells were seen gathered in bunches, or scattered singly among the spindle cells of which the tumor was made up. Curiously enough, ganglion cells

could not be demonstrated in the metastases only by virtue of the undifferentiated cells. Lederer states that the absence of differentiated cells in the metastases is the chief reason for the occurrence of errors in diagnosis, since the picture usually resembles some form of sarcoma. The condition, in his opinion, is not infrequent, and a more common knowledge of its symptomatology would disclose its presence more often. The roentgenogram of the metastasis resembles closely that of a periosteal sarcoma.

B. M. Fried.

Malignant Tumors of the Suprarenal in Children. P. A. Bendixen and F. H. Lamb, J. Lab. & Clin. Med. **12**:130, 1926.

Malignant tumor in suprarenal medulla is not unusual. In the majority of cases an orbital hemorrhage is the first sign observed, and it may occur before any tumor is palpable. The orbit first involved is often on the same side as the primary tumor. Diagnosis should not be difficult once the orbital hemorrhage has occurred; the disease is likely to be mistaken only for trauma, chloroma and scurvy. Metastases probably occur by way of the lymph stream, metastasis in the skin is rare. As the medulla of the suprarenal gland is neuroectodermic in origin, these malignant tumors are similar in their histologic structure to malignant neoplasms of the sympathetic nervous system, and may be designated as neuroblastoma.

S. A. Levinson.

1. Congenital Cirrhosis of the Liver. 2. A Chrondodystrophy. H. E. A. Boldero, Proc. Roy. Soc. Med. **20**:322 (Feb.) 1927.

1. Congenital cirrhosis of the liver occurred in a child, aged 21 months.

2. Chrondodystrophy was in a child aged 7½ years. On examination, she showed a painless bilateral deformity of the fingers. Roentgen-ray examinations showed an irregularity of the epiphyses of the middle phalanges of the second, third and fourth fingers of both hands and the phalanges were short and a little thickened. There was evidence of delayed ossification as the head of the ulna did not have a center. The history suggested an infective process, but the author believed the condition to be a rare generalized disturbance of bone growth.

Chronic Interstitial Nephritis: A Renal Dwarf. W. G. Wyllie, Proc. Roy. Soc. Med. **20**:326 (Feb.) 1927.

The patient, aged 11 years, measured only 43¼ inches (127 cm.) in height. Her weight was 45 pounds (20.4 Kg.). She showed a few skeletal deformities. The blood pressure was 110 systolic; 80, diastolic. The urine was pale and contained albumin but no casts. The blood urea was 171.6 mg. per hundred cubic centimeters. The maximum urea concentration two hours after she received 10 Gm. of urea reached only 1.5 per cent.

Williamson, New Orleans.

A Case of Sickle Cell Anemia in the Sudan. R. G. Archibald, Tr. Roy. Soc. Trop. Med. & Hyg. **19**:389, 1926.

A case of anemia associated with marked debility, pyrexia, slight jaundice, edema of the feet, enlargement of the liver and lymphatic glands, occurring in a native of the Sudan is described. There was a diminution of the red blood cells, leukocytosis, low hemoglobin percentage, a color index of 0.9, erythro-

blasts and phagocytosis of red blood cells. The most striking feature in fresh and stained preparations of the blood was the large number of elongated and sickle-shaped erythrocytes, averaging nearly 50 per cent. Hanging-drop preparations of fresh blood suitably sealed and kept at room temperature (31 C.) showed, after twenty-four hours, nearly 100 per cent of sickle cells. The sickling is apparently due to some inherent property of the cell, independent of any substance in the serum. The blood picture is identical with that of sickle cell anemia, a specific entity investigated by American writers. Clinical characters of the case corresponded to those of sickle cell anemia, differing only in the absence of lesion of the skin.

ARCH. PATH.

INVESTIGATIONS CONCERNING THE PATHOGENESIS OF INFANTILE ACIDOSIS. CALIXTO TORRES UMANA, Rev. franç. de pediat. **2**:717, 1926.

The author reports a syndrome existent on the high plateau of Bogota which affects infants under 2 years of age and is characterized clinically by persistent vomiting, severe depression and a frequently fatal outcome. There is a definite acidosis, the picture being like that of a diabetes with, however, no hyperglycemia. The primary cause is unknown but it would seem probable that there exists some infectious process evidenced by a leukocytosis with a polymorphonuclear increase. The author feels that the metabolic disturbances are aggravated by the high altitude, a relative anoxemia interfering with oxidative processes.

THE PYURIAS OF INFANCY. E. STRANSKY, Rev. franç. de pédiat. **3**:163, 1927.

In the first part of this article, the author discusses at length various studies on the pathogenesis of pyelitis, reviewing again the question of ascending or hematogenous infection. In the second part, he discusses forty-seven cases of pyuria which have come under his observation. Some of these developed in infants who were previously in good health; in others, a congenital abnormality of the urinary tract was shown at autopsy; many occurred in conjunction with a athrepsia, syphilis or diarrhea. A vicious circle is often established in which a diminished resistance prepares the way for an infection of the kidney; this in turn causes an anemia, which further lowers the resistance. Transfusion would seem to be a logical therapeutic measure, and the author reports several cases in which this was used with gratifying results.

LESLIE, Chicago.

PRIMARY CARCINOMA OF THE LIVER. H. ROSENBUSCH, Virchows Arch. f. path. Anat. **261**:326, 1926.

On the basis of a malignant adenoma of the liver of a male child, aged 8½ months, Rosenbusch discusses the origin of primary carcinoma of the liver. The tumor described was limited to the liver, but its malignant character was held to be established by invasion of the blood vessels of the liver. The lobulation of the liver was abnormal, which condition was considered evidence of developmental anomaly. Differentiation into solid cellular strands occurred, but did not result in the formation of typical liver cords. The stroma varied in density and ripeness, its proliferation having occurred not independently but as the result of the primary proliferation of the indifferent liver epithelium. Tabulation of thirty-two previously reported carcinomas of the liver in childhood leads the author to conclude that there is a gradual transition from mixed tumors

containing several varieties of tissue plus carcinoma, to tumors composed of epithelium alone, and that all have their origin in abnormalities of development. He postulates further that primary carcinoma of the liver in the adult also arises, not from previously differentiated cells which have undergone anaplasia, but from cells which have remained incompletely differentiated.

O. T. SCHULTZ.

ENDOCRINE SYSTEM IN OSTEOGENESIS IMPERFECTA. T. FAHR, Virchows Arch. f. path. Anat. **261**:732, 1926.

In his examination of a stillborn, full term, female child with osteogenesis imperfecta, Fahr paid especial attention to the endocrine system, in which he described changes that he interpreted as an abnormal maturity of the organs of the system. The suprarenals were smaller than is normal in the new-born, and the medulla was relatively more prominent and gave a marked chrome reaction. The ovary contained well developed follicles. The medulla of the thymus was prominent, whereas in the normal child from birth to the fifth year the cortical zone is more prominent. In the thyroid, follicle and colloid formation were present, and the piling up of the epithelium in places was suggestive of hyperplasia. In the hypophysis there were numerous eosinophilous cells and much golden brown pigment which gave the iron reaction. Only the parathyroids were free of changes which the author could interpret as evidence of precocious maturity. Kaufmann's theory of the congenital dysfunction of the osteoblasts as the cause of osteogenesis imperfecta, Bauer's theory of congenital dysfunction of all supporting tissues, and the possible thyrogenous origin are discussed. Admitting that dysfunction of the osteoblasts is evidenced by its results in the skeletal malformations, Fahr believes that abnormality of the endocrine system in the form of a precocious maturity which is not compatible with life may be the more important fundamental factor. A theory based on a single case is not always easy to uphold. In an addendum to his article, Fahr describes briefly the observations in a second case of osteogenesis imperfecta in which the changes in the endocrine system were less marked, although evidences of abnormal maturity were unmistakable (unverkennbar) in the suprarenal, thymus and thyroid. Wider experience in the histologic examination of the endocrine organs of new-born infants showed that well developed graafian follicles are not unusual at birth, that eosinophilous cells may be numerous in the hypophysis at this stage and that the endocrine system may be variable in apparently normal new-born infants.

O. T. SCHULTZ.

THE RÔLE OF TRICHOCEPHALUS DISPAR IN PATHOLOGY. W. TOBLER, Ztschr. f. Kinderh. **42**:324 (Nov.) 1926.

A case of massive infection with *Trichocephalus dispar* is reported in a boy about 4 years old, who suffered for months with an uncontrollable diarrhea, and was reduced almost to a skeleton. In direct examination of the stool, 6,000 eggs were counted to a square centimeter of surface. Death occurred from pneumonia, and by autopsy one *Trichocephalus* could be found buried in each square centimeter of intestinal surface in the large intestine, which meant that the number of worms must have exceeded 3,000. There was a complete lack of eosinophilic leukocytes in the blood in a count of 800 cells. The lack of these cells was not to be explained so much by a migration to the affected

large intestine, as by the assumption of a high-grade exhaustion of the depots of formation. The treatment of the patient with thymol and with injections of water with 10 drops of benzine was a complete failure.

Iron Therapy in the Anemia of Premature Infants. Lotte Landé, Ztschr. f. Kinderh. **42**:349 (Nov.) 1926.

An increase of hemoglobin was obtained in premature infants by the use of from 1 to 2.5 Gm. of reduced iron by mouth daily, this was associated chiefly with an increase of red cells in the first two or three months of life, a period when both values often sink to the lowest point. The large doses of iron were well tolerated. It was not possible to draw conclusions as to the etiologic significance of insufficient iron depots in the genesis of anemia in premature babies, since the nature of the activity of iron is unknown.

Myositis Ossificans in Childhood. Justus Neideck, Ztschr. f. Kinderh. **42**:427 (Nov.) 1926.

A case of myositis ossificans is described in a boy, aged 11 years, which began in his second year and which developed into severe general alterations typical of this disease in childhood. In connection with other cases in the literature, it is shown that this disease is a metaplasia, conditioned by the germ layers. A better name would be calcinosis.

Dry Pleuritis in Childhood. J. Fertig and A. Katzmann, Ztschr. f. Kinderh. **42**:530 (Dec.) 1926.

Specialists and general practitioners have given little significance to dry pleuritis, but it is a frequent disease of children and is often overlooked. On the basis of clinical signs, without a roentgen-ray examination, the diagnosis of dry pleuritis can be made in only half of the cases; but, etiologically, tuberculosis must be assumed in the great majority of cases. The diagnosis of dry pleuritis at the right time is of great clinical and prognostic significance. In all cases of acute disease in children with fever and without objective demonstrable changes, mediastinal pleuritis should be considered. Tracheo-bronchial adenitis is accompanied by periadenitis in the form of dry pleuritis.

Clinical and Experimental Data on the Treatment of Children with Diseased Kidneys. Felix Basch, Ztschr. f. Kinderh. **42**:589 (Dec.) 1926.

Among the many factors concerned in the exchange and excretion of water, not the least are the physical factors of different positions of the body; these can best be studied in cases in which there is a persistent retention of fluid and of excretion products, as happens in diseases of the kidneys. Hydrostatic pressure is a powerful obstacle to the excretion of water, and in relation to it rest in bed is advantageous; however, there are advantages in muscular action in ambulatory treatment if it is used with care and after the acute stage. When diuresis has not been caused by dietetic and medical treatment, mechanical therapy should be used; this should also be used in the case of continued hematuria and albuminuria. Harmful results from the use of these means are exceptional. In many cases the general condition, particularly the subjective condition of the patient, is improved. The appetite improves, diuresis increases — often greatly — and hematuria and albuminuria diminish and disappear. The duration of the disease frequently is shortened remarkably; the stay in bed is always shortened.

A Case of Pylorospasm Complicated by Malaria. H. Heinemann, Ztschr. f. Kinderh. **42**:672 (Dec.) 1926.

A baby in Sumatra developed a typical pylorospasm on the eleventh day. The temperature rose on the thirty-sixth day to 100 F. and on the thirty-eighth day to 102.4 F.; this was accompanied by desiccation and cyanosis and the passing of a stool with numerous red corpuscles. Organisms of tertian malaria were found in the blood. The patient's recovery followed the daily injection of 0.1 Gm. of quinine for six doses. Fever with pylorospasm is not unknown, but if it occurs in countries in which malaria exists, the organism should be sought. This is a serious complication in an infant. Emerson, Boston.

Normal and Subfebrile Temperature in Children. G. J. Huët, Nederl. Tijdschr. v. Geneesk. **71**:2064, 1927.

The author investigated the temperature curves (rectal temperature) in 330 children, in most of them during six months, and in all of them during at least three months. Of these children, more than 200 could be regarded as normal; one half of them had a positive, the other half had a negative, tuberculin reaction. The average daily deviation was the same in both groups. The highest temperatures most frequently found were between 37.3 and 37.6 C. (99.1 to 99.6 F.); the older the child, the lower the maximum temperature. A daily deviation of 0.8 C. (1.6 F.) could still be considered as being normal. To the lowest temperature little importance can be ascribed, as this (between 12 and 3 a. m.) has never been determined, and the temperature found depends on the time of the day when the temperature is taken. To study the diagnostic value of the subfebrile temperature, in a second group of 164 children the temperature was compared with the blood picture and the sedimentation rate of the erythrocytes. Between the different figures there appeared to exist some correspondence, though exceptions often occurred. The children of this second group all showed slight tuberculous deviations, but their temperature never was higher than 38 C. (100.4 F.). In children with an abnormal blood picture and an abnormal sedimentation rate, the temperature generally was a little higher; special stress is laid on the fact that in these children the temperature showed greater fluctuation and that the temperature curve was more irregular. The author thinks his results are of some value for the judgment of normal and subfebrile temperatures.

Van Creveld, Amsterdam.

## Nervous Diseases

The Infantile Type of Family Amaurotic Idiocy. Joshua H. Leiner and S. Philip Goodhart, Arch. Neurol. & Psychiat. **17**:616 (May) 1927.

Two cases of the infantile type of amaurotic family idiocy were reported with autopsy reports. Clinically, both cases presented the typical picture of the disease. Histologically, the brains differed from those in most of the infantile cases published by Schaffer and others in the absence of degeneration of the myelin sheath. In this respect, they strongly resemble the juvenile type.

Both cases showed a slowly progressive, chronic character. These observations do not correspond with those in cases recorded in the literature in which marked fatty degeneration and complete destruction of the nervous parenchyma occurred. Only mild changes were found in the basal ganglia.

Typical blastodermic (ectodermal) selectivity was found in both cases. Segmental selectivity was not uniform in character; in case 1 the cerebral hemispheres were more involved and in case 2, the cerebellum.

Both cases reveal varying degenerative processes involving different portions of the neuron. This holds true for the different components and elements of ectodermal origin of the central nervous system. In the entire group of infantile types of amaurotic family idiocy a variety of subgroups with mutations are found in the pathologic picture. The connecting links in this group are the ectodermal selectivity and the different degrees of Schaffer's type of cell degeneration.

THE MICROSCOPIC ANATOMY OF INFANTILE AMAUROTIC IDIOCY. ROY R. GRINKER, Arch. Path. **3**:768 (May) 1927.

The author reports the microscopic pathologic anatomy in two cases of amaurotic family idiocy in which early changes were revealed, and in which the development of the characteristic pathologic condition could be studied in its successive stages. In case 1, the patient died at the age of 22 months and in case 2 at the age of 17 months. Grossly, both brains were of normal size but distinctly hard. The convolutions revealed many gross abnormalities in position and size, and they were asymmetrical in both brains. The brains retained their shape as though hardened in formaldehyde for weeks, and cut with greatly increased resistance. The only gross alteration noted on the cut surface was the similarity of color of the gray and white matter. Careful microscopic studies with special reference to the early cell changes and the intracellular lipoids showed that the initial nuclear swelling and hyperchromatic appearance, the development of lipoid at the base of cells of normal size, which contained their full quota of Nissl bodies and normal neurofibrils and the gradual invasions of the cells by lipoids were the earliest pathologic abnormalities. Later the visible cytoplasmic reticulum degenerated, and still later the intracellular neurofibrils.

The fact that normal cells may be seen later in the course of the disease, and that transition stages to the final disintegration of the cell can still be seen, give rise to the belief that the brains, although they contained gross developmental defects, were composed of morphologically normal cells at birth.

The behavior of the lipoids was similar to that characteristic of senile changes in the cells, and suggested a composition of the intracellular material in amaurotic idiocy similar to that of senile lipochrome. The gradual development of a slowly increasing amount of intracellular pigment resembling senile pigment in a brain with congenital defects makes it more than likely that the process is a premature senile change in the cell. It is probable that primarily the cells are of normal morphology, and that after a variable period of apparently normal functioning, they undergo a pathologic process similar to senility in its slowness and ultimate lipoid product.

PARMELEE, Chicago.

•

ENCEPHALITIS AND ITS EFFECT ON THE BEHAVIOR OF CHILDREN: 1. A STUDY OF POSTENCEPHALITIC BOYS IN A HOSPITAL SCHOOL. DR. DANIEL H. FULLER, Atlantic M. J. **30**:350, 1927.

Physicians connected with the Pennsylvania Hospital are undertaking a study in the rehabilitation of youthful sufferers from encephalitis. The patients were carefully selected with regard to age, and severe neurologic disorders were excluded. The program of training consisted of school, manual training, farm-

ing, gymnastics and particularly supervised recreation. Conduct was stressed before everything, and daily reports were turned in on each student. Repression and discipline were necessary at first but later became superfluous as the boys fitted into their environment. Penalties consisted in deprivations, being put to bed, meals alone or an hour or two in the bath tub. Corporal punishment, having failed at home, was never resorted to. Rewards for good behavior consisted in trips here and there and special privileges. "One of the most effectual punishments is the ignoring, for a half-day, of the culprit who has broken a rule or disgraced himself by some misconduct."

A court, composed of the group with one person as judge, arouses the boys' sense of fair play and makes its penalties more effective. The formation of new habits is a slow process, and the labor involved extremely great, but the results appear to be promising.

DIAGNOSIS OF POSTENCEPHALITIC CONDITIONS. DR. EDWARD A. STECKER, Atlantic M. J. **30**:352, 1927.

Twenty-four boys and six girls, ranging in age from 18 months to 14 years were studied carefully in the months and years following the acute disease. Disturbances in behavior were of wide variety and usually of marked intensity. In only four of the group did serious behavior difficulties fail to develop. "Furthermore, the troublesome and dangerous behavior is not at all the result of deficient or defective intelligence. In only two of the cases in this series was there mental retardation. The change involves the personality of the child and practically reverses it, but spares the intellectual processes. It has been predicted that encephalitis may make a class of super-criminals." The acute symptoms were no reliable guide, for they might be trivial and the behavior outrageous. Usually, however, children over 16 or 17 did not succumb to these disorders The development of paralysis agitans was usually associated with mild conduct disorders, but in those patients who showed other neurologic phenomena the behavior was but slightly better than in those who escaped neurologic damage.

CHRONIC EPIDEMIC ENCEPHALITIS. P. K. MCCOWAN and J. S. HARRIS, J. Ment. Sc. **73**:300 (Jan.) 1927.

This paper reports work at the Maudsley Hospital on the effect of scopolamine on carbohydrate metabolism. The injection of $\frac{1}{100}$ grain (0.00065 Gm.) of scopolamine hydrobromide into a normal person brings depressant effects immediately and remotely. The same dose in encephalitic parkinsonian patients brings the same immediate but widely different remote effects. The drowsy period is shorter and is followed by improvement in the neurologic signs and in mental alertness. The effect of the same dose on the blood sugar curve of normal persons was a general inhibition of both the rise and the fall. In thirteen cases of parkinsonism the effect was depression of blood sugar levels with acceleration of the fall, an approach to the normal with a corresponding clinical benefit. In seven cases of encephalitis without parkinsonism there were results such as followed the injection of scopolamine in the normal person, with no clinical benefit.

Long distance treatment over two years has been tried with benefit and without the development of tolerance. Often $\frac{1}{100}$ (0.00065 Gm.) is given hypodermically in the morning with two or three similar doses by mouth during the day. Increase of comfort is obtained with no effect on the course of the disease.

BOND, Philadelphia.

THE MANAGEMENT OF MENTAL DIFFICULTIES IN A PEDIATRIC CLINIC. BRONSON CROTHERS and MARGARET WIRT, M. Clin. N. Amer. **10**:1251 (March) 1927.

A trial of various plans designed to meet the problem of the management of mental difficulties in their pediatric clinic convinced the authors that much may be accomplished without elaborate personnel and unlimited time. Absolutely essential, however, are pediatricians who are interested, and are willing to spend time and energy in the study of such cases, and a social worker with psychiatric training. More effective cooperation can usually be established between mothers and the pediatrician who has the general care of the child, than with the psychiatrist. Her loyalty to the former enables him to exercise an authority over the child's habits which in many instances may to a considerable extent counterbalance the specialized knowledge of the latter. It seems probable that ultimately greater good will be accomplished for the greater number if at least the preliminary work is done by pediatricians and social workers rathers than by immediately referring all children with mental difficulties to special clinics. After such a preliminary study, many cases will be found which will obviously require more specialized attention than can be given in the general clinic. These are referred to clinics in which more formal study is possible, the transfer being more easily made and more willingly accepted as a result of the previously established loyalty to the pediatrician.

The benefits of the plan accrue not only to parents and patients. To the pediatrician, the importance of the problems of mental difficulties is made clear, and the futility of careless advice becomes evident. Attempting to do the work himself, he comes to a realization of the complexity of some of the problems and to the value of useful consultation with others. The authors conclude that most of the mental and emotional difficulties of childhood can and should be cared for by pediatricians, always granting that pediatricians are industrious, patient and eager students of the "whole child."

SMITH, Ogden, Utah.

CHRONIC HYDROCEPHALUS WITH REPORT OF CASE APPARENTLY ARRESTED. CHARLES K. FULLER, Canad. M. A. J. **17**:675, 1927.

The author advises the ligation of two common carotid arteries to decrease the amount of cerebrospinal fluid formed by the choroid plexus. In case the intracranial pressure increases or remains the same after the ligation, he advises ligation of one of the vertebral arteries.

The case reported occurred in an infant, aged 9 months, with a diagnosis of chronic obstructive hydrocephalus (congenital). Ligation of the left common carotid artery was performed above the omohyoid muscle and ten days later the right common carotid artery was ligated in similar position.

The improvement began at once. Two years later, the infant seemed perfectly normal mentally and physically.

MOORE, Omaha.

HEMIPLEGIA OF SUDDEN ONSET. E. CAUTLEY, Proc. Roy. Soc. Med. **20**:317 (Feb.) 1927.

The case reported was in a boy, aged 5½ years. He was well on October 30, but was restless during the night and was unable to stand or to move the left arm and leg the next morning. There was no fever. The mother had had four miscarriages and was under treatment for syphilis when the boy was admitted to the hospital on October 31. On admission, the boy was drowsy and looked ill, and his speech was slurred and defective. The

cerebrospinal fluid was under slight pressure and was a little turbid; dextrose was present but diminished; the polymorphonuclears were 65 per cent and the lymphocytes were 36 per cent. The Wassermann reaction was positive. The disks were pale and anemic. In a few days after admission the mental condition became normal but the hemiplegia remained marked. The liver, tonsils and lymph nodes were enlarged. The author reported this case in the hope of eliciting views as to diagnosis.

WINGED SCAPULA. T. TWISTINGHAM HIGGINS, Proc. Roy. Soc. Med. **20**:321 (Feb.) 1927.

The case reported was in a boy, aged 6½ years. The condition was not noticed until two weeks after an injury to the right shoulder and arm. Was it a traumatic lesion of the nerve of Bell? Was it an old standing poliomyelitis? Or was it some form of myopathy?

The case was reported to elicit a diagnosis. WILLIAMSON, New Orleans.

MORISON LECTURES ON MENTAL DEFICIENCY. R. D. CLARKSON, Edinburgh M. J. **34**:19 (Jan.), 61 (Feb.) and 200 (April) 1927.

Three lectures on this subject given before the Royal College of Edinburgh are found in these numbers of the *Edinburgh Medical Journal.* The author modestly disclaims any hope of increasing the knowledge regarding mental deficiency, but wishes to lessen the confusion which is present in the terminology and in the unsettled problems connected with this extensive subject. Clarkson states that there is at present no satisfactory definition of the mental development of individuals whereby they may be exempted from deficients. He discusses the historical classification, the English and Scotch legal definitions of idiocy, imbecility and feeblemindedness, and the medical nomenclature. Most of these are defective in that they pertain to adults rather than to childhood. The psychologists have helped some in the definition of mental deficiency by the development of measures for determining the intelligence. Clarkson uses chiefly Terman's modification for the Binet tests, but he believes that no test can be devised to distinguish between the mental defectives and the normal, for individuals are not only deficient "in ability to make acquirements" but are even more unable to use them "when they are made."

Physical stigmas, such as microcephaly and mongolism, are of diagnostic value in a few instances, but psychic stigmas are more important. Mental deficiency is a symptom of many diseases, such as injury of the brain or defects of development, but classification on pathologic grounds tends more to be a test of the pathologic conditions associated with the defective mentality.

The author's opinion is that mental deficiency cannot be satisfactorily defined, but that it consists of an inability to form associations of ideas which may be measured by Binet's tests, or in a lack of one or more of the twelve primitive instincts that are essential to normal human conduct and development, and commonly in both of these deficiencies. In adult life, the state may be graded by the capacity for useful work and the persistent impulse to earn a living.

The causes of mental deficiency are discussed in the second Morison lecture in the February number of the *Journal.* Clarkson regards Fredgold's classification into fourteen groups as the most useful. The three primary groups are the simple, microcephalic and mongolian. Seven secondary groups are the syphilitic, amaurotic, hydrocephalic, parencephalic, sclerotic, paralytic and a group due to toxic inflammatory or vascular changes. Four secondary types

are caused by defective nutrition of the brain, among these the epileptic, cretinoid, blind and deaf. The author thinks it difficult to decide whether some cases are primary or secondary, especially in injury of the brain at birth when there has been "a restricted potentiality for cerebral development" which makes the brain more susceptible to damage.

The author stresses the point that in most secondary cases "there is no relation between the physical signs and the degree of mental defect." He believes that some cases are not recognized as primary until signs appear at maturity. Microcephalus furnishes usually less than 1 per cent of institutional defectives, while from 5 to 10 per cent are Mongolians. The latter type is discussed from the standpoints of age of the parents, influences of worry and anxiety, as, for instance during the World War, and the effect of syphilis. He believes that the cause of mongolism is unknown, though the defect is in the fertilized ovum.

The author discusses at length the influences of heredity as advanced and criticized by many recent authors. In his practice, he states that he has seen little difference between the parents of defectives and those of normal children. In conclusion as to the causes, he believes that it is not known how mental deficiency is produced in most cases, that it is usually spontaneous, not dependent on a neuropathic diathesis nor transmitted according to mendelian laws. Aments or normal children may come from normal or defective families.

The third and final lecture is in the April number, and deals with treatment. Mentally defective persons should be treated, trained and cared for, to allow them to become useful, disciplined, to avoid vice and be less of a wasteful public expense. When cared for in their families, they "diminish the social efficiency of their normal relatives." The three objects of treatment are to make the defective as efficient as possible, to protect the community in an economic way, and to prevent deficiency from occurring.

The health of the affected person should be improved as it offers more chance of permitting the mind to become developed. Surgical care will often help the spastic paralytic patients. The cretins are benefited if the condition is recognized and treatment begun in the first year of life. The common practice of using thyroid extract in Mongolians is without benefit.

Education of the mentally deficient cannot be attained by simply keeping the child longer in school as is the case with more nearly normal children. Native reactions or instincts must be present in a person before education can modify them. Praise, imitation, modification of pugnacious impulses, pride, ownership, constructiveness, handwork and supervision by a nurse or teacher who has a real affection for these children are all useful in modification of instinctive dispositions and in furthering education.

Clarkson advises for mothers the use of Dr. John Thomson's book, "Opening Doors." Defective children have little of the feeling of satisfaction which a normal child gets from the experience of trial and error, but this can be increased by proper praise and encouragement. Stimuli from without may be supplied by play, and character and intelligence are developed by it. Instructors in this do not need long training, but they should have a natural adaptability for teaching such children to play.

Attempts at training the memory can only be useful if the meaning of what is memorized can be understood. Not much time should be spent in teaching the three R's. The child can often be taught some useful handicraft, and a child who is not suitable for ordinary school instruction should not be kept in schools for more than two years in spite of pressure from the parents.

Institutional training is recommended for those who cannot go to special schools, as they are better off in institutions than in the competitive environment of normal children. They should be placed there early in life. Some defectives have a demoralizing effect on the character of other members of the family, and if they are kept at home they may cause a breakdown in the health of the mother. The medical profession has the responsibility of deciding whether a given patient is suitable for training, and most physicians see so few patients that they do not know the problems of the mental defectives. Children who cannot be taught to earn their own living are suitable for institutions, in which they can be made more independent and less burdensome to their families. They have continuous care, which is impossible in the short daily hours of the special school. Institutions are far too few. Trades and occupations are best taught in a large establishment with a capacity of 500 or more, though units of small houses for 50 or 60 children can advantageously be placed around a central administrative building. Continuous care, from birth to death, in the same institution is useful, as defectives are incapable of adapting themselves to new situations.

The prevention of deficiency is only partly possible. Improvement of public health, temperance, reduction in venereal diseases and better midwifery are helpful. Sterilization of defectives is impracticable as it is impossible of being carried out. Defectives are rarely the children of mentally similar persons. Sterilized defectives cannot be turned loose because of the danger of spreading venereal diseases and of the trouble to the community. They are happier in an institution in which they have the company of others, and in which they may receive praise for whatever work they can do. Early detection, improvement of health, educational measures, useful work, happiness, contentment, protection of community and reasonable cost for their care make up the treatment which these unfortunates should receive.

NEFF, Kansas City.

THE SYMPATHETIC SYSTEM OF THE CHILD. JEAN MINET, LE MARC'HADOUR and PIQUET, Rev. franç. de pediat. **2**:687, 1926.

In an attempt to study the vegetative nervous system of the child, the oculocardiac and the solar reflexes were determined in 112 cases. Normally one expects a slowing of the pulse rate when pressure is made on the eye, and a diminution in pulse pressure when pressure is made over the epigastrium. The amount of slowing or diminution may be considered as an estimate of the local vagus or sympathetic excitability. It was found that antagonism between these two reflexes is relatively rare. They are usually both exaggerated or both are slight. The authors conclude that the study of these reflexes, although showing local excitability, is not of value in determining the existence of a vagotonia or a sympatheticotonia.

LESLIE, Chicago.

EXPERIMENTAL RESEARCH ON THE PATHOGENESIS OF HYDROCEPHALUS. E. D'ABUNDO, Neurologica **5**:257 (Oct.) 1926.

The author tries to elucidate experimentally the complicated question of the pathogenesis of hydrocephalus. In his three series of experiments followed by hydrocephalus, he deals first with subcortical lesions, which resulted in the formation of cysts in direct communication with the ventricular cavities. In the second series, the resulting cyst was separated from the lateral ventricle by means of a more or less thick layer of nervous parenchyma; in the third series, he deals with ligature of the right carotid artery which was followed

by a localized area of softening in the brain. In the second series, in which no direct lesion of the ventricular wall was produced, the hydrocephalus was due, according to the author's view, to the vascular hyperemia which he was able to trace and which was the expression of the inflammatory reaction following the operation. The hyperemia might have influenced, directly or indirectly, the formation of the hydrocephalus. According to the author, the inflammatory lesions play an important part in the mechanism of the formation of hydrocephalus in cases involving the ventricular walls, either directly or indirectly.

From the pathologic point of view, the most important observations were the subependymal gliosis, shown by the presence of numerous astrocytes, and the lesions of the choroid plexus, shown by the presence of swollen and vacuolated cells of the secretory epithelium. The anatomic lesions were marked in from seven to eleven days after the operation, and showed a tendency toward regression in cases examined twenty-five days later. For the intimate pathogenesis of hydrocephalus the author invokes, besides the circulatory changes, other factors that should be investigated further.

FERRARO, New York.

MENINGITIS CAUSED BY FRIEDLÄNDER'S BACILLUS. F. PAPANDREA, Pediatria. **35**:371, 1927.

Two cases are described. In both, the spinal fluid was turbid and mucous, and the Friedländer's bacillus was obtained in pure culture. The first case, that of a girl, aged 5 months, at autopsy presented a bilateral, fibrinopurulent pleurisy, bronchopneumonia of the left lower lobe, fibrinopurulent pericarditis and purulent leptomeningitis. *Bacillus mucosus-capsulatus* was recovered from all lesions, and the meningitis was clearly part of a septicemia.

The second patient also died, but did not come to autopsy. Clinically other lesions were not noted, and the author is inclined to consider the meningitis as primary. The only therapy attempted in both cases was intravenous administration of methenamine.

CURE OF PNEUMOCOCCI MENINGITIS IN AN INFANT. U. SALA, Pediatria. **35**:492, 1927.

A boy, aged 8 months, with a negative family and past history, had been seized two days before admission with fever and restlessness alternating with stupor and vomiting. Physical examination disclosed nuchal rigidity, a positive Kernig sign and other symptoms of meningitis. Lumbar puncture brought out purulent spinal fluid, containing many pairs of gram-positive diplococci, chiefly extracellular. The infant's mother refused to allow intraspinal treatment, and recourse was had to the intramuscular administration of polyvalent antipneumococcic serum. Two doses of 20 cc. and 25 cc., respectively, were given the first day, and a dose of 20 cc. daily for the next two days. Improvement began after the second dose, and the baby had recovered completely ten days after admission.

SALA, New York.

CHARACTERISTICS AND FATE OF MONGOLIAN IDIOTS. RUNHILT V. D. STEINEN, Heidelberg, Monatschr. f. Kinderh. **35**:495, 1927.

A study was made of eighty mongolian idiots seen during the years from 1911 to 1926. The average number, which from 1911 to 1919 was from three to four a year, doubled after 1920. The only explanation is the injurious effect of the war. As many boys as girls were affected, and, as other authors have

reported, the affected child was from the seventh to the fourteenth child in families with many children, or was born from seven to fifteen years after the last child in smaller families. These figures support the idea that exhaustion of the mother is an important etiologic factor.

Of the forty-six children who died in this series, 27 died during the first years of life; 13 from the second to the sixth year; 2 from the seventh to the tenth year; 2 from the eleventh to the twentieth year and 2 after the twentieth year. The children showed a tendency to suffer from catarrhal inflammations and bronchopneumonia. Only 4 per cent lived after the twentieth year.

The author then discusses the physical and mental characteristics of these children, but tells nothing new.

THE CLINICAL PICTURE OF MYATONIA CONGENITA. SOFIE KATZ, Berlin, Monatschr. f. Kinderh. **35**:517, 1927.

The author reports seven cases of this unusual disease. These cases had the following points in common: (*a*) In none was there any history of the disease in the family; (*b*) in none of the children was there any disturbance of intelligence; (*c*) in none was there disturbance of sensation; (*d*) all showed abdominal breathing; (*e*) in all the disease started shortly after birth.

The cases differed in the degrees of muscular contracture. For instance, in one there was a complete hypotonia; in others, in addition to hypotonia, the feet were held in abnormal positions; in a third group, contractures involved the hands and arms. All observers have noted the contractures of the arms in which pronation is so marked as to cause the hands to be turned out.

Pathologic examination showed atrophy of the muscle fibers and in two cases, changes in the spinal cord. Whether the disease is related to the muscular atrophy of the spinal type, is as yet unsettled.

GERSTLEY, Chicago.

ENCEPHALOGRAPHY IN CHILDHOOD. P. DANNENBAUM, Ztschr. f. Kinderh. **42**:578 (Dec.) 1926.

It may be said that encephalography has proved itself of value in the study of children as a process which helps the observer to make valuable diagnostic conclusions and to gain a deeper insight into cerebral conditions, and often leads to the diagnosis of an abnormal cerebrum. The reading and understanding of encephalograms gives experience and practice, and the publication of as many as possible of the cases that come to autopsy appears to the author to be of great importance for the recognition of individual pictures of disease. He believes that this method is relatively without danger if it is used only in the clinic and with prudence and skill.

A VENOUS MURMUR IN THE HEAD, A PECULIAR LOCALIZATION. W. LÜTJOHANN, Ztschr. f. Kinderh. **42**:680 (Dec.) 1926.

When the mother of a healthy, well developed infant, 7 months old, put her ear against the child's head, she heard a singing noise which increased in the course of a month. Over the whole area of the scalp one could hear an uninterrupted murmur synchronizing with the heart beat, increasing and diminishing. It was heard best over the small fontanel and there was no variation when the baby was in a lying or a sitting position. The heart was normal, and the blood did not show anemia. It must be assumed that there was some sort of abnormality of the saggital sinus, perhaps a narrowing near the small fontanel.

EMERSON, Boston.

ALTERATIONS OF THE SKULL IN EPILEPSY AND IDIOCY WITH CONSIDERATION OF THE OSSIFICATION OF THE SUTURES. MARTERNA, Verhandl. d. Deutsch. path. Gesellsch. **21**:333, 1926.

Alterations of the skull are frequently found in idiocy and epilepsy. They were observed in 40 per cent of the epileptic patients and 60 per cent of idiots after exclusion of the alterations which appeared after the cessation of bony growth. The premature synostoses of the sutures were the most frequent alteration in epileptic patients, while microcephalic patients had the first place in idiots. Partial premature ossifications of the sutures were present in 22 per cent of the epileptic patients and in 19 per cent of the idiots. These synostoses did not interfere with the growth of the skull in the direction vertical to that of the synostosis. Many of the synostoses were interpreted as the result of a primary trauma of the brain, but there were also cases in which the synostoses were the primary alterations and possibly the cause of the epilepsy (primary synostotic epilepsy).

WILHELM HUEPER.

PATHOLOGIC AND HISTOLOGIC OBSERVATIONS IN THREE CASES OF COMA DYSPEPTICUM. YOSHIRO YAMAOKA, J. Pediat., Tokyo **321**:172 (Feb.) 1927.

The author reports three cases of severe dyspeptic coma, clinically identical with those described by Heubner under the name of coma dyspepticum, with careful microscopic studies. All the patients were girls, aged 7, 4 and 3 years, respectively. The general conclusion of his observations may be summarized as follows: 1. There was no morphologic relation between this condition and the so-called thymicolymphatic tendency, as there was no demonstrable enlargement of the thymus or lymph glands. 2. In all three cases, there was a fatty infiltration in the parenchymatous organs, especially in the liver and the spleen. This fatty substance was for the most part neutral in reaction, but it was intermingled with a lipoid substance which gave a positive reaction with the Smith-Dietrich method. This high degree of fatty infiltration appeared to be a secondary product due to metabolic disturbance, rather than a causative factor in the disease. 3. The fatty substance found on the mucous membrane of the stomach in all three cases might be due to the absorption of the gastric contents. 4. In the splenic pulp, certain foci were seen which appeared to contain hyaline and connective tissue substances. This is not a characteristic of the disease but is worthy of note.

KATO, Los Angeles.

## Diseases of the Eye

A CASE OF MULTILOCULAR CYST. COHEN and MEEKER, Arch. Ophth. **56**:211 (May) 1927.

The right eye of a colored boy, aged 4½ years, became proptosed, following a blow, without sign of hemorrhage, redness or pain. The child was poorly nourished, and the blood Wassermann reaction was four plus. Antisyphilitic treatment was carried out for four weeks without effect on the exophthalmos. Five weeks after the appearance of the first symptoms, the orbit was opened by a Kronlein operation, exposing a bluish, ovoid, fluctuating mass attached to the outer side of the optic nerve, near the optic foramen. Following removal of the tumor, the exophthalmos disappeared. Because the authors believed that only tumors formed of, or producing, lymph vessels should be called lymphangiomas, they prefer the descriptive term "multilocular cysts of the optic nerve meninges," of which their case was an example.

WESCOTT, Chicago.

REPORT ON A CASE OF BILATERAL GLIOMA OF THE RETINA. CURED IN THE NON-ENUCLEATED EYE BY RADIUM TREATMENT. MARK J. SCHOENBERG, Arch. Ophth. **56**:221 (May) 1927.

The author says that the case of bilateral glioma of the retina which he reports is the first one on record in which a patient, treated by radium and observed for ten years, recovered useful vision, and in which a cataract was successfully removed. The peculiar reflex from the left pupil was noted by the mother when the child was 1 month old, but nothing was done about it for two years, when an examination revealed the vitreous humor filled with the gliomatous mass. The left eye was removed and, while under ether, a complete examination of the other eye was made. Glioma was found and radium treatment started. Two years later, opacity of the lens was noted, and eight years later a cataract was removed, with vision of 15/100.

WESCOTT, Chicago.

## Diseases of the Ear, Nose and Throat

PERORAL ENDOSCOPY: ITS USE IN COMPLICATIONS FOLLOWING OPERATIONS ON THE NOSE AND THROAT. GABRIEL TUCKER, Arch. Otolaryng. **5**:321 (April) 1927.

Tucker reports fourteen foreign body cases due to accidents following otolaryngologic operations, observed in the examination of 1,750 patients with foreign body cases at the Chevalier Jackson bronchoscopic clinics. All the patients made uneventful recoveries following peroral endoscopy with removal of the foreign bodies. The cases included: (1) lamp from a Whitehead mouth gag in the right bronchus, (2) catch from a tonsil forceps in the right bronchus, (3) tonsil snare wire in the right bronchus, (4) gold tooth crown in the right bronchus, (5) four cases of deciduous tooth in the right bronchus, (6) deciduous tooth in the left bronchus, (7) tonsil sponge in the left bronchus, (8) portion of nasal rasp in the left bronchus, (9) intubation tube in the left bronchus, (10) wooden applicator and swab in the right bronchus and (11) radium capsule in the stomach. Eleven of these cases were seen in the last year, which Tucker attributes to the increased recognition by physicians of the true nature of such conditions.

In addition the author reports four cases of pulmonary abscess following tonsillectomy in which bronchoscopy was performed. Three patients received treatments bronchoscopically at intervals, with complete recovery. The fourth patient had a pulmonary abscess not advantageously placed for bronchoscopic treatment and was referred for operation.

The article is concluded by calling attention to the need in large hospitals in the great medical centers for fully equipped bronchoscopic clinics with specially trained otolaryngologists to render assistance in diagnosis and treatment of diseases of the lungs, esophagus and stomach.

GIBSON, Chicago.

ACUTE INFECTIONS OF THE NASOPHARYNX AND ITS ADNEXA IN INFANCY AND EARLY CHILDHOOD. JOHN LOVETT MORSE, M. Clin. N. Amer. **10**:1143 (March) 1927.

Acute nasopharyngitis is one of the most common as well as one of the most potentially dangerous diseases of early life. Proper hygienic care, with avoidance of exposure to contagion and removal of adenoids at any age will greatly diminish its occurence. Treatment should be instituted early. The child should be isolated, put to bed, and weak organic silver solutions and bland oils instilled

into the nose. Ethmoiditis probably complicates most cases of acute nasopharyngitis in early life. It may be suspected if the symptoms are unusually severe, if the eyelids are puffy, if the discharge is unilateral and evidently comes from high in the nose, and if it persists during convalescence. Infants and children do not have otitis media unless they have adenoids or acute nasopharyngitis. Moderate reddening of the drum with distinct landmarks does not demand operation unless the temperature is high and there is much pain. The indications for incision are marked bulging of Schrapnell's membrane or of the drum as a whole; a localized nipple-like bulging, or a thickened hazy, yellowish tympanum. If the discharge persists for three or four weeks, the cause is usually adenoids or extension to the mastoid. Mastoiditis seldom develops if otitis media is recognized early and the drum incised. Fulness of the posterior wall of the external auditory canal and enlargement of the posterior auricular gland are important but not infallible signs. No doubt many cases clear up without operation if there is free drainage from the middle ear. However, if the symptoms are at all marked or are increasing, operation should be done at once. Morse states that in Boston and its vicinity, the frequency and virulence of mastoid infection has increased during the past twenty or twenty-five years. Extension of the inflammation to the lateral sinus and meninges is more common in early childhood than in infancy, and is usually, but not invariably, preceeded by inflammation in the mastoid. The symptoms of sinus thrombosis may be indefinite, but irregular temperature and leukocytosis are suggestive, and chills are almost positive proof. Meningitis is a rare complication of otitis media in early life, and the symptoms are those common to all forms of purulent infection of the meninges.

Morse tersely summarizes his contentions as follows: If infants and children are properly taken care of and protected against contagion, they will not have acute nasopharyngitis. If they are put to bed and properly treated when they have acute nasopharyngitis, they will seldom develop otitis media unless they have adenoids. If otitis media is recognized early and the drum incised, extension to the mastoid is unusual. If mastoiditis is recognized early and the mastoid process opened, extension of the inflammation to the lateral sinus seldom occurs.

SMITH, Ogden, Utah.

SARCOMA OF THE NASOPHARYNX IN A CHILD WITH INTRACRANIAL INVASION. BRINDEL, RETROUVEY, GUINAUDEAU, Rev. de laryngol. **3**:101 (Feb. 15) 1927.

Malignant tumors of the nasopharynx are rare in adults but exceptional in the infants. In 70,000 patients examined in the Clinic at Bordeau in twenty years, thirty-four were observed; only three occurred in patients under 30 years of age. A case was reported in a boy, aged 7, who had a sarcoma of the nasopharynx and was under observation in the children's ward for six months. The mother was also in the clinic for a disarticulation of the hip because of sarcoma of the femur.

Autopsy showed that both hemispheres were intact. A lobulated tumor about the size of a goose egg occupied the center of the base of the cranium. There was a prolongation into the left orbit. The right orbital cavity was entirely filled. The hypophysis was invaded, and there was involvement of both anterior and posterior clinoid processes. There was invasion of the nasal fossae, ethmoid and sphenoid. The pathologic condition was that of fibrosarcoma.

The literature does not have much bearing on the heredity of malignancy. The history in the present case showed both mother and child in the hospital at the same time, and both had sarcoma.

Irradiation with the roentgen ray was tolerated well except for the initial shock. The bones of the cranium offered resistance to the rays, and could the tumor have been excised as in the larynx, it is possible that the radium may have accomplished more promising results.

ROTH, Kankakee, Ill.

A CASE OF MASTOIDITIS DUE TO PLAUT-VINCENT ORGANISMS. L. LETO, Pediatria. **35**:241, 1927.

A girl, aged 7, had had otitis media in December, 1924, for which ossiculectomy had been performed. Prolonged treatment did not result in a cure, and the patient reentered the hospital in May, 1925. Mastoidectomy was then performed. The antrum was full of creamy, greenish-yellow, foul-smelling pus, and the walls were necrotic. Whereas at the first operation, the pus contained only ordinary pyogenic organisms, with a predominance of diplococci, the pus at the time of the mastoid operation contained an overwhelming number of fusiform bacilli and *Spirilla*. The postoperative treatment consisted of dressings soaked in a 20 per cent solution of arsphenamine in glycerin, and good results were obtained.

ADENOID VEGETATIONS AND ENURESIS. E. DI LAURO, Pediatria. **35**:437, 1927.

There is no apparent causal relationship between the coexistence of adenoids and enuresis. If present, the vegetations must be removed to prevent their evil systemic effects, but there is no justification in promising a cessation of the enuresis in a child with adenoids after these have been removed.

SALA, New York.

## Diseases of the Skin

A PURIFIED COAL-TAR OINTMENT FOR THE TREATMENT OF INFANTILE ECZEMA. MARQUE O. NELSON and ARNOLD E. OSTERBERG, Arch. Dermat. & Syph. **15**:669 (June) 1927.

The authors have found that that fraction of coal tar which is obtained by steam distillation is as effective in the treatment of infantile eczema as the original crude tar. The distilled product does not stain and is less irritating than the crude tar.

ACTUAL SUPERFICIAL THERAPY BY "GRENZ" (INFRA-ROENTGEN) RAYS. GUSTAV BUCKY, Arch. Dermat. & Syph. **15**:672 (June) 1927.

Rays of about 2 Angström units are entirely harmless. They are completely absorbed by the upper layers of the skin. With waves of this length the author has treated successfully several varieties of eczema, acne rosacea, lichen planus and pruritis ani. Several other skin diseases, including infections and tumors, reacted well. The possible indirect effects of these waves on internal organs is discussed. In one case, the acute symptoms of gastric ulcer disappeared almost instantaneously.

JEANS, Iowa City.

THERAPEUTIC ASPECTS OF INFANTILE ECZEMA. LEON H. DEMBO and J. EDGAR FISHER, M. J. & Record **125**:552 (April 20) 1927.

In the treatment for any disease, the first principle involved is the removal of the cause, if it is known. In the therapy of infantile eczema, the suggested removal of the cause is of little value, since this is not known. For this reason,

the authors confine themselves in their article to the question of treatment. In their series they grouped their cases into five distinct types: papulovesicular, squamous, erythematous, seborrheic and neurodermatitic. The squamous type predominated. The treatment given was divided into four kinds: (1) local, (2) roentgen-ray, (3) dietetic and (4) special treatment (drugs and endocrine products). Each kind is discussed, and the results obtained in their cases are given.

In analyzing results, the authors believe that one should be extremely conservative in pronouncing patients cured. In their opinion, a year should be placed as a minimum period of observation. More knowledge of the etiology is necessary before any great progress in the treatment of this condition can be expected.

WILLIAMSON, New Orleans.

MULTIPLE SUBCUTANEOUS SARCOMATOSIS IN AN INFANT. G. LATTES, Pediatria. **35**:476, 1927.

At the age of 3 months, the child developed two nodules on the forehead, each the size of a lentil. When seen at the age of 8½ months, there were seventy-six such nodules, scattered over the scalp, the upper part of the arms and the trunk. The lower part of the limbs, forearms and hands were free. The nodules varied in size from that of a lentil to that of a hazel-nut; they were subcutaneous, and the skin over them was normal.

Histologically, the two nodules examined consisted of parenchyma and stroma, the latter exclusively vascular. There were large cellular nests; the cells at times were round but usually they were ovoid or elliptical; they were situated deep in the dermal structures, often near the sebaceous and sweat glands, and at first separated from one another by connective tissue. As these nests grew larger, they coalesced and completely invaded the subcutaneous connective tissue. Atypical karyokinesis was noted repeatedly. The cells were generally round or polyhedral in these larger nests; they varied in size, though they were usually small; they had large round nuclei surrounded by a thin rim of protoplasm.

Hypodermic administration of arsenic was of no avail. At the time of this report, the child was gradually failing, and new nodules were beginning to appear all over the body.

SALA, New York.

MONGOLIAN SPOTS IN A TWIN. LUDWIG SILBER, Ztschr. f. Kinderh. **42**:674 (Dec.) 1926.

Silber reports a case of mongolian spots in one of twins of the same sex; the other remained free after six months of observation. Biopsy showed typical cells. This occurrence is hard to explain and is published in the hope that, with other cases, it will help to solve the problem as to whether or not these spots are hereditary.

EMERSON, Boston.

AMOUNT OF IODINE IN SUBCUTANEOUS TISSUE IN SCLEREDEMA. S. KOYANAGI, J. Pediat., Tokyo **321**:197 (Feb.) 1927.

The author found that the amount of iodine in a 11 months old baby who died of marasmus was 56.59 per cent; in a 6 day old baby with scleredema it was 38.3 per cent. These figures agree with those obtained by Knöpfelmacher in 1897. The author concludes that the amount of iodine contained in the subcutaneous tissues of an infant with scleredema is the same as that of a normal infant providing the age is the same.

KATO, Los Angeles.

## Surgery and Orthopedics

THE PATHOLOGY AND TREATMENT OF THE RETAINED TESTIS IN CHILDHOOD. A. H. SOUTHAM and E. R. A. COOPER, Lancet **212**:805 (April 16) 1927.

In general, it may be stated that unilateral or bilateral cryptorchidism occurs, roughly, in five subjects in every thousand, and is often associated with a hernia of the inguinal type. Though the condition may cause little trouble during childhood, it may be a source of considerable irritation later in life, not only from the abnormal anatomic position of the organ, but also from secondary complications, and doubt as to its ability to function.

Ten retained testes were obtained by operative procedure; two from adults, the rest from children. From a study of these, the authors came to the following conclusions:

The further the preadolescent testis has descended in its normal route the more closely does it correspond to the scrotal gland of the same age. Glands arrested in the abdomen were affected by different degrees of fibrosis and a greater reduction in the germinal elements. At first there was an "apparent," later an "actual," disappearance of the tubules. No abnormality in the structure of the epididymis was found. Double cryptorchidism in both man and animals is associated with aspermatogenesis. It is surmised that the retained testis develops normally during early postnatal life, but later if it does not reach the scrotum, it undergoes retrogressive changes.

Spontaneous descent is not common after the first three years of life. If the testis has not reached the scrotum by the age of 3, that is the time of election for operation. The retained testis is more liable than the normally placed organ to undergo malignant degeneration. The presence of a living testis in the scrotum in a considerable percentage of cases justifies the performance of the operation. The indications for operation are:

1. In the authors' opinion cases of iliac retention (least common type) are not suitable for transplantation to the scrotum, as a general rule. If bilateral, it is justifiable to try to bring one testis down.

2. In the high scrotal group, in which the testis has escaped just outside the external abdominal ring, operation is rarely necessary.

3. The inguinal group comprises the largest number of patients, and all should receive operative treatment, i. e., transplantation of the testis into the scrotum.

LANGMANN, New York.

INTUSSUSCEPTION WITH PARTICULAR REFERENCE TO THE ACUTE VARIETY IN INFANTS. LAMBERT ROGERS, Practitioner **118**:4 (April) 1927.

The two most common intra-abdominal surgical emergencies in children are pyloric stenosis and intussusception. Four types are described: (1) ileocecal, the most common; (2) colic; (3) enteric and (4) ileocolic.

The frequency in early life is due to several factors: first, developmental, namely, undue mobility of the cecum and colon; second, hyperirritability of the bowel; third, swelling of the lymphoid tissue in relation to the ileocecal junction.

As a rule, the onset is sudden, and well nourished healthy babies are more often affected than ill nourished ones, and boys more often than girls. The commonest age incidence is between 5 and 9 months. The child is quiet except when having attacks of great pain. Passage of blood by rectum and vomiting are constant factors. A sausage tumor may or may not be felt, but on rectal examination the typical "red current jelly" is expelled.

Surgical operation is urgent. Treatment by water pressure is not without danger. It is important to give subcutaneous injections of physiologic sodium chloride solution or a transfusion of whole blood to help the patient through the operation. Atropine is given beforehand, and gas and oxygen or ether as an anesthetic. If the intussusception is reducible, it is well to put an interconnecting stitch between the cecum and iliac fossa to prevent recurrence. If the bowel is gangrenous, resection and performance of an end to end or lateral anastomosis is the procedure of choice.

For the first few days following operation a rise in temperature frequently occurs. It is essential to keep the child warm and to administer plenty of fluid. Aperients are avoided for four or five days. In conclusion, it is stated that intussusception, the commonest surgical emergency in infancy, should be suspected in babies who, between intervals of lying quiet, draw up their legs and scream, vomit and pass blood by rectum.

The mortality from intussusception in infants has been high during the past. It is rapidly diminishing, and there is only one way of maintaing this improvement, namely, by early diagnosis and operation when the condition has progressed to a stage at which reduction is possible.

GELSTON, San Francisco.

TUBERCULOUS DISEASE OF THE SHOULDER JOINT. NORMAN M. DOTT, Edinburgh M. J. **34**:46 (March) 1927.

The author reports a boy of 9 who had been disabled for four years previously following an injury to the right shoulder from a fall. The pathologic condition was a typical "caries sicca" with muscular atrophy, shortening, deformity, and restriction of the mobility. A sinus was present at the posterior border of the deltoid. Dott then operated on the shoulder, exposing the diseased area and removing the head and upper fourth of the humerus and the axillary border of the scapula. He cut a slot in the shaft of the humerus to fit over the edge of the scapula and secured them by suture and a plaster dressing. One year later, the local and functional results were satisfactory in spite of the shortening.

OPERATION FOR HYDROCEPHALUS IN A BABY. JOHN FRASER, Edinburgh M. J. **34**:47 (March) 1927.

An infant, aged 7 months, had a normal head until 2 months of age, since when it had increased steadily in size. Fraser discussed the causes and varieties of hydrocephalus. In this case, he attempted to affect the balance between the production of cerebrospinal fluid and the reduced absorption by the leptomeninges by removing the choroid plexus of one ventricle as has been suggested by Dandy. Fraser showed the patient at 1 month after the operation, which was well tolerated and which resulted in a lowering of the intracranial tension, and a diminution in the circumference of the head.

ACCESSORY TARSAL SCAPHOID. W. A. COCHRANE, Edinburgh M. J. **34**:52 (March) 1927.

A girl of 10 years had weakness and fatigue of the feet, and pain in the region of the scaphoid, the symptoms existing for six months. Both feet were pronated, and a bony tender prominence was present in the region of the scaphoid eminence. The tendons of the tibialis posticus became prominent

on forced inversion of the feet. A roentgenogram showed an accessory scaphoid bone. Treatment for flatfoot has caused some improvement.

The author discusses Zadek's operation for removal of the accessory scaphoid, and the need for differentiating this abnormality from a fracture of the scaphoid.

A Simple Method of Intestinal Anastomosis. Norman M. Dott, Edinburgh M. J. **34**:55 (March) 1927.

This surgeon offers an additional method to the thirty-one different procedures already suggested. Eck's method of experimental venous anastomosis is applied to intestinal surgery for lateral and end-to-side anastomoses. The technic is described. It is of interest to pediatricians because of the end-to-side ileocolic anastomosis for congenital megacolon. Among the patients shown or reported are two children, aged 13 years and 18 months, respectively. The former had congenital hypertrophy of the colon. The latter had an acute ileocolic intussusception at 4 months of age, and was operated on on the fifth day of the disease. Operation was successful in both instances, and the recovery uncomplicated.

Neff, Kansas City, Mo.

A Contribution to the Study of Vesical Lithiasis in the Child. V. Mikulowski, Rev. franç. de Pédiat. **3**:210, 1927.

Three cases of vesical calculi are reported; two occurred in children with an arthritic heredity, and the third was probably infectious in origin, occurring with a pyelitis. There were symptoms of interrupted and painful micturition and a fever out of proportion to the constitutional disturbance. The condition in the infectious case and in one of the arthritic cases, in which an anti-arthritic diet was also given, cleared up on alkaline therapy. In the third case, that of an infant 10 months old who died of a tuberculous meningitis, the calculi (urates) were discovered at necropsy.

Leslie, Chicago.

Acute Vertebral Osteomyelitis. A. Bocchini, Pediatria. **35**:554, 1927.

A girl, aged 8, fell on her buttocks about two months before admission. She was able to arise unassisted, and for the next few days complained only of moderate intermittent pain over the last vertebrae. The parents, however, noted a curvature on walking, which persisted.

Two days before admission, the child was suddenly seized with chills, fever and severe pain over the lower part of the vertebral column. On examination, a marked rigidity was found over this region, with exquisite tenderness. The child could not walk, efforts at bending were poor, and the vertebral column was maintained rigid. Two days after admission, death ensued.

Autopsy revealed a hemorrhagic osteomyelitis of the bodies of the second and third lumbar vertebrae. Necropsy having been performed thirty-four hours after death, bacteriologic studies were not attempted, but the histologic preparations showed some small gram-positive diplococci, barely visible.

Sala, New York.

Report of a Case of True Diffuse Varices. Herbert Orel, Ztschr. f. Kinderh. **42**:668 (Dec.) 1926.

In this case genuine diffuse varices were displayed soon after birth in the left lower extremity and on the penis. They caused considerable swelling of the soft parts at the knee and in the region of the ankle in connection with

indirectly demonstrable widening of the deep-lying veins. The appearance of the skin in a half-sister of the patient, which may be essentially of the same nature, speaks for the hereditary condition of the disease. There is no reason for designating any kind of trauma as the cause. Whether the right-sided facial paralysis was called forth by analogous formation near the central nervous system, remains undetermined. The high grade weakness of vision was caused by astigmatism of both eyes.

Noteworthy is the marked similarity of this observation, especially in regard to localization, to the case of Heide. The widening of the varices is not so enormous as in the 12 year old boy of Heide, but it is probable that in the course of years it would reach the same dimensions. The freedom from abnormality of each definite skin area in this case and the one cited should be especially mentioned. The regions affected may correspond to parts of metameres defectively organized.

A Case of Retroperitoneal Hernia with Miliary Tuberculosis. Liebers, Ztschr. f. Kinderh. **42**:676 (Dec.) 1926.

A girl, aged 3, had vomited since birth, and complained of pain; at eight weeks the vomiting increased, the vomitus becoming green. The abdomen was soft and sunken on the sides. Tuberculous meningitis was suspected, and at autopsy miliary tuberculosis was found; there was also a retroperitoneal hernia composed of the whole small intestine. The chief signs, according to Lichtenstein, are circumscribed, globe-shaped distention of the umbilical region, with a sinking in of the area corresponding to the colon, and the palpation of a definite elastic spherical mass. With prompt recognition of the condition, patients have been known to recover. Ninety cases have been reported.

Emerson, Boston.

## Miscellaneous

Value of Ultra-Violet Ray Therapy in Childhood. Frederick F. Tisdall, Canad. M. A. J. **17**:667, 1927.

The author reviews briefly the physics of ultraviolet radiation and summarizes the various claims as to its therapeutic usefulness.

In order to obtain a fair judgment as to the actual value, various representative hospitals in Canada and the United States were visited and the results summarized. The conclusions were:

1. Ultraviolet therapy is an absolute specific in the treatment of rickets and tetany. 2. Definitely beneficial results are obtained in treatment of abdominal, mediastinal and glandular tuberculosis. The results are questionable with bone, joint and pulmonary tuberculosis. 3. It may be useful as an adjunct in treatment of psoriasis, chronic eczema, furunculous, seborrheic dermatitis, alopecia areata, purpura, celiac disease and malnutrition. In most cases, however, it can well be replaced by more simple forms of therapy.

Moore, Omaha.

Settlement Houses. J. J. A. Loehnis, Rev. internat. de l'enf. **3**:209, 1927.

The conception of the modern settlement can be traced to LaPlay and other French writers of his day, but the first unit actually incorporated was founded in London by Canon Barnett, in 1873, and named Toynbee Hall after one of the Canon's enthusiastic disciples. At present there are sixty-six of these

institutions in Great Britain, most of them, of course, being located in the poorer districts of London. The object of these centers is, first, to attract scholars, teachers and social workers who will take up residence in these neighborhoods, and by precept and example, kind encouragement and sympathetic cooperation, raise the standard of living among the so-called submerged tenth. Social reforms have emanated from these settlements to the great advantage of the people, morally, physically and economically.

From this modest beginning, the idea of the settlement has developed until it now embraces the civilized world. In Germany, the Sociale Arbeitsgemeinschaft has broadened the original plan so as to include a system of clubs in which laborers and students may meet on terms of mutual help. In the Scandinavian countries there is a strong religious element incorporated in the various programs, while in Holland special effort is directed toward supplying for its laboring element suitable recreation for hours off duty. The French settlements are dedicated particularly toward the elevation of family life. The elemental ideal of love and charity in personal service, however, remains the same in all countries.

AMESSE, Denver.

PHYSIOLOGIC AND PATHOLOGIC CHEMISTRY OF THE TEETH WITH SPECIAL REFERENCE TO THE INFLUENCE OF CALCIUM, VITAMINS AND PARATHYROID GLANDS. GUTTORM TOVERUD, Supp. to Norsk Tandlægeforenings Tidende, 1926, p. 145.

This is the report of an experimental study on rats in the course of which it was found that the chemical composition of the teeth may be influenced by deficiencies of diet and by functional disturbances of the parathyroids.

ARCH. PATH.

# Society Transactions

## AMERICAN CHILD HEALTH ASSOCIATION

*Fourth Annual Meeting, Washington, D. C., May 9, 10 and 11, 1927*

SELECTED ABSTRACTS OF PAPERS

*Monday, May 9, Morning Session*

WHAT THE AMERICAN CHILD HEALTH ASSOCIATION IS DOING. Dr. Samuel J. Crumbine.

The American Child Health Association aims to acquire and to put at the disposal of other voluntary agencies and governmental departments information that is of value in advancing the cause of child health. Obviously, such information must be of both a scientific and an administrative nature. Affirmative action in public health on the part of any government must be conditioned, in the main, on the people's general level of intelligence regarding public and personal health. This in turn depends on the voluntary health agencies that mold public opinion through education and demonstration. Voluntary agencies are able to do pioneer work. "It is, therefore, in the fields of survey, research, demonstration and interpretive promotion work that the American Child Health Association finds its greatest usefulness."

The association has cooperated with official agencies in the nation wide campaign for clean and safe milk. (Here, with the approval of the State Department of Health and the State Dairy Commissioner, a survey is made of actual conditions. An expert points out defects in methods and equipment and offers suggestions for betterment. Then comes the phase of interpretation of the results of improved conditions). In cooperating with the schools, the Health Education Division did valuable work in stimulating the schools to accept the responsibility of looking after the health of the children. From surveys that the schools made of their own problems, material was sifted and prepared and sent to secondary schools, describing the problems in health education and the procedures that seemed to work best in meeting these problems. The association only undertakes problems that have more than local interest, which are in a sense new or which have failed to develop properly because of lack of sufficient consideration of certain phases.

Among the most significant achievements of the association may be mentioned the following: A health survey of eighty-six cities with a population of from 40,000 to 70,000 and of eighty-three cities with a population of more than 100,000 yielded information and so focused attention as to set forward public health practices at least a decade. With the school problems particularly, the organization serves as a clearing house of inquiry and information. At present there is research under way to weigh and measure the effectiveness of the health programs in the schools of the country. Since 1918, five educational conferences have been held, to which were brought representatives of different professional groups. Recently, the Division of Health Education has assisted in the development of two international congresses on health education and, on request, has acted as agent in

editing, publishing and distributing their proceedings. The statistical report on infant mortality was in several instances the means of bringing about much needed reorganzation of local health work.

The association has lent experts to state departments of health to assist them in enlarging the area of birth registration. Expert personnel has been sent to aid in the education and control of midwives among negroes in southern states. Health educational literature prepared by the association has been considered by the Editor of the *Journal* of the American Medical Association to excel in soundness of scientific statement and in effectiveness of presentation. Grants of money have been made by the association to develop projects which seemed of significance and which without the subsidy might have remained undeveloped indefinitely. One of these grants, which helped to provide for trained Indian nurses among the Chippewa Indians, has resulted in a permanent Indian Health Service financed by the Minnesota State Legislature. A grant was also made to the Joint Committee on Material Welfare to stimulate interest in improving the conditions surrounding maternity and early infancy. Another grant was made for studies determining what constitutes health in the normal child and what deviations from normal may be properly disregarded. In addition, fellowships and scholarships are given to those who show particular interest and ability in problems of health education.

The association is not one which seeks prestige for itself. If the time comes when its usefulness in the field of child health is over, because of wise spread knowledge in matters pertaining to health and efficient government administration, it will turn its resources into new channels.

---

*Monday, May 9, Afternoon Session*

CHILD HEALTH IN THE PAST. Dr. Philip Van Ingen.

This paper was published in full in the AMERICAN JOURNAL OF DISEASES OF CHILDREN. (**34**:95 [July] 1927).

---

*Tuesday, May 10, Evening Session*

THE SCHOOL AND CHILD HEALTH

IMPORTANCE OF BRINGING THE CHILD TO SCHOOL IN GOOD HEALTH AND KEEPING HIM IN GOOD HEALTH DURING SCHOOL LIFE. Dr. Borden S. Veeder.

It may well be asked why "school" should be an objective for maintaining the health of the child. The "school" is only one of the environmental factors which influence development and certainly cannot be regarded as a goal or an aim in life. That the importance of health to the developing child has its basis in a much bigger and broader ground, no one would question. Nevertheless, "school" plays such a dominating rôle that it has an importance in the problem of individual health.

For the first few years of a child's life, his environment is closely limited to his immediate family group. His development depends largely on the character and personality of a few persons. The induction into school life marks the first definite change in his environment.

To expect that a child shall make these new adjustments is to ask a great deal. To ask a child in poor health from malnutrition or from some definite

physical disease or defect to do this is to ask too much, as experience has all too frequently shown.

Let us consider the physical condition of children at the sixth year, or when school life begins for the vast majority. Statistics vary somewhat but, taken as a whole, there is a surprising agreement in regard to the observations. Among the most important are malnutrition, 30 per cent; carious teeth, 60 per cent and obstructed nasal breathing, 25 per cent. These vary in degree, and it is the degree of the defect that makes it of little or great importance to the welfare and health of the child.

As the child grows older, there is a gradual decrease in the percentage of handicaps, as a rule, but new and important forms play an increasing rôle. Thus, the extent of cardiac disease and of defective vision increases year by year as the school age advances. It has been estimated that 75 per cent of the children in school have one or more physical defects. Certainly not more than a third of these, however, have conditions which to any appreciable extent affect the general health and progress.

For the average child, the induction into school life means the almost certain exposure to the infectious diseases of childhood. The child whose health is below par is not any more susceptible to these infections than the child in the best physical condition—contrary to the usual layman's point of view—but the child physically fit will come through them, as a rule, without difficulty and is not apt to develop complications that prolong the injury of the disease. The greatest damage, however, does not come from the specific group of communicable diseases, but from the group of nondescript infections of the upper respiratory tract which are the chief cause of trouble among school children and the major cause of absence from sickness. Children with impaired health, and particularly those in whom obstructed nasal breathing is present not only are more susceptible to such diseases, but experience more serious obstruction to their progress and development from the colds that are so common as a result of exposure in school.

Of the effect of ill health on progress in school and the question of retardation, it is surprising to find how little definite information there is regarding this point, which is of seemingly fundamental importance. The nearest conclusion is that somewhere around 10 per cent of the children in elementary schools (and this figure is probably low) are definitely retarded and have had to repeat one or more years. To what extent this retardation is due to physical reasons is difficult to say. Various estimates of from 10 to 40 per cent have been made. I do not think it can be doubted that it plays an important rôle. Every physician can recall striking cases in which apparent mental backwardness was not due to mental defect, but in reality was the result of some correctable physical handicap.

The child who for physical reasons is unable to enter into the usual play and activities of his schoolmates not infrequently develops traits or tendencies that are detrimental in the development of what one may call his personality. When one finds a child who fails to fit in, whether the cause is due to retardation, physical limitations or even exceptional ability, one finds an unhappy child.

It has often seemed to me, as I have discussed schools and education with my pedagogic friends and child health with my friends who are interested in child hygiene that the means and mechanisms are too often considered as an end and are not looked on in their proper function. What all are interested in is the life of the child. Both the physical and mental development go hand in hand, and neither is of secondary importance.

A Survey of the Health Program in the San Francisco Schools from 1921 to 1927. Dr. Harold K. Faber.

The health program in the San Francisco schools dates back to a survey made by the San Francisco Tuberculosis Association in 1921. It was found that among the 44,500 children in the grammar grades of the public schools, 21 per cent were 7 per cent or more underweight; 40 per cent showed poor posture, 87 per cent large adenoids and 35 per cent enlarged cervical glands. As the state law does not permit removal of the clothing for examination, other defects may have been overlooked. This study gave the initial impetus to a campaign to improve the health of the school children. The campaign was supported largely by the Tuberculosis Association with the idea that each department of work would be transferred to the city authorities, the Board of Health and the Board of Education, as soon as it had passed the earlier developmental stages. Three methods which seemed to give promise of success in combating malnutrition were started together. These were nutritional classes, midmorning lunches and health education. (Ten nutrition classes were started in 1921.) Thorough physical examination of the underweight child was urged, but could not be enforced. In 1923, 1,232 children were enrolled, and individual consultation supplemented instruction in the classroom. In 1924, the Board of Health began to take over the work and has had complete charge of the nutrition classes since 1925. One of the advantages of this is that the public health nurse is able to go into the home, and so better appreciates the needs of the child. Statistics among children in the nutrition classes up to 1925 showed little improvement in the nutrition index. In 1925, a special investigation of 182 of these children was made and corrective measures, such as tonsillectomy, were carried out. Survey of habits showed that many of the children drank coffee and had insufficient sleep. In 1925, the policy of selecting children for the nutrition classes by the height-weight standard alone was abandoned, and children showing 10 per cent or more underweight were examined by school physicians who decided whether or not the children should be admitted to the classes. It is essential that the malnourished child be examined individually, but even with this, unless the recommendations advised are carried out, little can be accomplished. The importance of this is shown by a comparison of two groups: one in which the carrying out of the recommendations was optional with the children and their parents, and the other, an open air class, in which the recommendations were actually carried out. In the first group, 35.4 per cent showed a poorer nutritional index; 29.3 per cent remained stationary, and only 35.3 per cent showed actual improvement. In the second group, none showed a loss; 6 per cent remained stationary and 94 per cent showed a gain.

Milk lunches in the middle of the morning were first served in December, 1921. This is voluntary except for the fresh air classes and seems to supply a demand. In reply to the criticism that this lunch interferes with the appetite for lunch, Dr. Faber feels that there are many children who go breakfastless and who need their caloric requirements filled. If this is the case, it would seem more logical to supply these children with milk as soon as they get to the school. In comparing three schools in which the mid-morning lunch is given with three in which it is not taken, the percentage of 10 per cent underweight children has decreased in six years by 5.2 per cent in the first group and by 4 per cent in the second group. The difference is not striking. In addition to the mid-morning lunch, many schools now have their own cafeterias.

Health education in the pedagogic sense was confined in 1921 to three schools that served as demonstrations. In 1923, the program was adopted by the Board of Education for introduction into all schools. Health is not taught as a separate subject, but as incidental to the teaching of the regular subjects. The children seemed interested in the subjects and the teachers have an impression that there is a general improvement in the personal hygiene. Children have a knowledge of and a pride in health unthought of a decade ago, and the level of general intelligence in matters of health and hygiene is being definitely raised.

CHILD HEALTH PROTECTION OR NEGLECT: THE ULTIMATE COST TO THE COMMUNITY. Louis I. Dublin, Ph.D.

In 1900, the mortality of infants in the death registration area was 169 per thousand mid-year population or 17 per cent of all infants counted in the census of that year. In 1925, the figure was more than 75 per thousand mid-year population, or between 7 and 8 per cent. This figure is an average for the country as a whole. The 1925 statistical report of infant mortality issued by the American Child Health Association shows that of the 697 cities reporting, 190, or 12.9 per cent, still had rates of mortality in excess of 100. On the other hand, there were eight communities with rates as low as 35 or less. The cities in the Pacific Coast States have had low rates for years, with few exceptions. Many eastern cities do almost as well. The number of infant deaths per year in the United States is now 180,000.

In the last twenty-five years, the mortality of children from 1 to 4 years of age has declined from 21 to a little more than 6 per thousand. This mortality can be reduced to 2 per thousand. Between the ages of 5 and 9, the mortality has declined from 5.1 per thousand in 1900 to 2.1 in 1925. This can be reduced to 1 death per thousand. Between 10 and 14 years of age, the mortality has declined from a little more than 3 per thousand in 1900 to a little under 2 in 1925, and this also can be reduced to 1 death per thousand living at those ages.

Such reductions, when accomplished, will save 110,000 infants annually. In addition, 34,000 children between 1 and 4, close to 11,000 between 5 and 9 and about 7,500 between 10 and 14, or counting all under 15, a total of 162,500 a year, may be counted on.

The cost of our preventable child mortality can be estimated in dollars and cents. The wastage in children under 1 year brings about a loss of $1,175,000,000 a year, and for children under 15 years of age, the loss reaches $2,200,000,000. This is the amount that the country would ultimately gain if these lives were saved and were allowed to reach maturity and play their part in the nation's work. The most conservative estimate of the cost of illness among children cannot be less than $5.00 per child per annum. This would mean a total of close to $200,000,000 a year as the approximate cost of medical, nursing and other care of children during illness.

Most parents are ill-informed as to the hygiene of infancy and childhood and are unable to cope with the situation which the conditions of life in American cities have brought about. The congestion is so great, the proximity of persons so continuous and the opportunities for cross-infections so constant that the problem of keeping children well is not so much one for the individual parent as it is a community problem for common solution. The keynote is not cure but prevention.

The first year of life is the most fruitful for preventive effort. It is then that the largest number of children die unnecessarily. Through a demonstration lasting little more than three years, in the small Canadian town of Thetford Mines, the rate of infant mortality was reduced from close to 300 in 1920 to 79 in 1926.

The Maternity Center Association made available to pregnant women the facilities of its welfare clinics, in which qualified physicians gave advice and also sent nurses to the homes. As a result, the rate of premature infants was reduced to 4.8 per thousand births, whereas in the general population in the City of New York, the rate in the same year was about three times as high.

After the first year, when the conditions of early infancy, such as diarrhea and enteritis and pneumonia have done their work, diphtheria, whooping cough and tuberculosis are the principal destroyers. Every one of them is certainly capable of considerable reduction. It has been demonstrated to the hilt that deaths from diphtheria are unnecessary and can be prevented.

Tuberculosis follows diphtheria as the most important of the communicable diseases of childhood. The demonstration at Framingham, Massachusetts, while not primarily directed at the children, has shown that they, more than any other group, favorably responded to what was done in the community.

An investigation made by the American Public Health Association, shared also by the American Child Health Association, has shown that in the larger cities not more than 59 cents per capita was being expended annually for what might be classified as child health work in its various branches. It is not known how much more is spent by the nonofficial agencies, but in many communities these private organizations are active, and if they do not spend as much as health departments, they spend a considerable fraction of this sum. It is safe to say that in the general run of American communities, from 75 cents to a dollar per capita would more than cover all of the expenditures that could possibly be allocated to this branch of community health service, whether official or nonofficial.

The health agencies of typical American communities are not well enough organized to conduct adequately the work for the protection of children. In an outline of an ideal health department prepared by Professor Winslow of Yale University, it was assumed that an expenditure of just under $1.50 per capita, if properly administered, in a well organized department would serve to carry on the activities for child welfare in a modest but effective manner. Possibly a more liberal expenditure, more like $2.00 or $2.50 per capita under present conditions, will be found necessary. However, what an absurd contrast exists between these minimal sums of what is required per capita to conserve child life and the value of the child when its life and health are endangered by neglect.

---

*Wednesday, May 11, Afternoon Session*

## THE MEDICAL SCHOOL AND CHILD HEALTH

### Experience with Courses in Preventive Pediatrics

Dr. Borden S. Veeder, Washington University School of Medicine, St. Louis: The subject for this discussion is the medical school and child health. Despite all the work that has been done by states and municipalities, by far the greater number of children are under the care of their private physicians.

The medical man in the past has been trained almost entirely to think in terms of disease. In recent years there has been a change in the feeling of men who have been teaching in the medical schools, leading to the point of view that the subject of preventive medicine and health must be stressed.

In the School of Medicine at Washington University with which I am connected, from a prescribed curriculum, which was strictly adhered to and which

took all the time of the student, we have been changing to an elective system that leads up to a point in the last year when a large part, almost one half, of the senior year is purely elective.

With the necessity for cutting down the number of hours in each subject, we are not able to give as much preventive pediatrics as we would like or feel is desirable. The students do not begin pediatrics until the third year, when they receive a series of formal lectures, about ten of which are given on the subject of normal growth and development. The same year they have a course that is called "physical diagnosis," which is in reality a study of the normal child as compared with the abnormal. In this course the student must examine children, determine the state of nutrition, etc. These courses are compulsory. In the fourth year, the students attend one clinic a week. In this course, talks on psychology, behavior problems and the like are included. One morning a week for one sixth of the year is spent in the wards of the Children's Hospital. The pure hygiene work, which includes a discussion of methods in welfare clinics, comes under the Department of Hygiene. This is not satisfactory as a whole, because the modern student is becoming interested in approaching medicine from the standpoint of health.

One of the most interesting things has been that 75 per cent of the men in the senior class have elected pediatrics as one of their elective courses. About 20 per cent have taken the maximum number of hours, and a large part of this time is spent in the outpatient dispensary, where they obtain individual work in the Well-Baby Clinic.

Several years ago, we instituted a month's work in postgraduate education for men who have been out in practice. For the past three or four years, we have had the maximum number of men we will take—somewhere between 65 and 70 a year from all parts of the United States and from foreign countries. In this course, we give something of the preventive point of view of pediatrics. The students receive two lectures a week throughout the four weeks, and go directly into welfare centers for two hours a week. In addition, they receive a certain amount of training in the normal growth and development of the child. I have been much gratified to receive letters from a number of these men who have gone back into the small communities from which they came and to learn that at least 10 or 15 per cent of them have become definitely interested in child hygiene work and measures since they have returned to their own communities. We do not attempt to turn these men out as specialists in pediatrics, but they go back home with the idea that pediatrics is something different from treating the child when it is sick. One thing that has interested me in talking with these men has been the answer to the question, "Why did you come here and give up a month at your own expense to study pediatrics?" They are men who have been out of medical school for from fifteen to twenty-five years. Almost without exception the answer is something like this: "The people in my community are demanding something of me in connection with their children I cannot give. Somebody has got to give it, and as I am interested in children, I want to learn what this thing is." It is a fact that the people at large have demanded of these men something in regard to the guidance of their children that is more than simply the care of the child when he is sick.

Dr. Richard M. Smith, School of Public Health, Harvard University, Cambridge, Mass.: There are two different methods of teaching medicine as there are in general education. One method tries to cram the student's mind with a great mass of information. The other attempts to give only the essential facts

concerning any subject, and devotes its major energies to training the student to think, and to use efficiently the facts at his disposal. The Harvard Medical School is definitely committed to the latter method of teaching.

Child health may be considered under two important divisions: Preventive pediatrics, so-called, and community organization. Preventive pediatrics includes all the things that are done for the individual child to secure for him every known advantage for normal development and prevention from disease. Community organization is concerned with the functions of public and private agencies, looking toward the protection of the health of children, and is a part of the general program of public health.

The first endeavor in teaching child health is to create a point of view on the part of the student which will make him appreciate that interest in and work with normal infants and children are essential parts of medical practice. This attitude is made easier because of the fact that a considerable number of the men who are teaching the undergraduate students are themselves actually engaged in conducting conferences for infants and children and are therefore concerned with the supervision of well children, in addition to taking care of sick children in the hospital and in private practice. This arrangement is possible because of the plan of the Boston City Health Department whereby the medical personnel of the child conferences conducted by them is provided by the pediatric departments of the medical schools in the city.

Numerous methods of giving to undergraduate students definite instruction in child health have been tried in the past. In general, it has been found that they have not progressed far enough in their medical training to appreciate a presentation of the details of community organization.

We therefore content ourselves with giving to them one lecture in the third year, in which this phase of child health is discussed in outline.

There is an elective system, also, at Harvard, but the student must choose certain things. He must plan one month of medicine, one of surgery, one of pediatrics, and one month of obstetrics. The rest of the time is free. In the one month required in pediatrics, the students spend one afternoon a week in different city health clinics. They are taught the care of the normal child, and they acquire a general understanding of the methods used in dealing with children in groups. Throughout the curriculum, the care of the normal child and the prevention of disease are emphasized. Provision is made for resident postgraduate study as a Fellow in Child Hygiene. The person holding this appointment spends his mornings in the hospital clinic and his afternoons in field work. He has direct supervision of the medical aspects of the city child hygiene work done in the stations for which we are responsible. He is brought in contact with many of the phases of this work in its administrative details. He also does some of the teaching in the clinics, which the fourth year students attend, and gives some lectures in the graduate courses.

In the School of Public Health, there is an intensive course in child hygiene offered, which occupies the entire time for one month. The various aspects of work for children are presented through lectures and visits to nearby institutions. This course is elected by certain members of the fourth year class who are preparing for work in public health. It is attended largely by special students as a postgraduate course, or as part of a longer course of study, looking toward a special degree.

We also offer in June a special postgraduate course in the Medical School. In this course, as in the course at Washington University, the care of the normal

child is emphasized, and a certain amount of information is given on the aspect of work with children which is strictly in regard to child hygiene.

We also furnish opportunity for work in the city health clinics to our residents and interns in the hospital, so that they come directly in contact with work for well children, and a certain amount of contact with the organized work that is being done.

For students desiring to investigate some special phase of child health, opportunity for research is open in connection with the School of Public Health.

Child health is considered as one division of pediatrics. We think that the undergraduates can be taught little of the details of the work. They can, however, get enough insight into the subject to appreciate its possibilities for further study. The graduate student who wishes to specialize in child health should be well grounded in pediatrics by work beyond that offered in the undergraduate curriculum.

Dr. Harold K. Faber, Stanford University, Calif.: For five years Stanford University has offered an elective course in preventive pediatrics. It serves merely as an introduction to the subjects discussed, but at least it opens the eyes of the students to the really amazing development and the present enormous scope of the child welfare movement. The course begins with a review of prenatal problems; the relation of the family to the child; economic and social factors; school laws; widows' pensions; orphans and the children of the handicapped; the handicapped child; the control of contagious disease. A lecture follows on vital statistics, then one on prenatal care in its various aspects. Two lectures are devoted to the general milk supply and its control and to certified milk. As a rule, the class is taken on a tour of inspection to a certified diary. A review follows of such phases of child hygiene as milk stations, visiting nurse organizations, the work of the Metropolitan Life Insurance Association, well baby centers here and abroad, foundling homes, health centers for older children, visiting new mothers in the home, care of the preschool child, protective inoculations, care of the teeth, corrections of defects of the eye, ear, nose and throat; posture, mental testing and the problems of the mentally defective child. Another lecture is given on teaching health in the schools with a description of the various methods in use and a discussion of nutrition classes, midmorning lunches and so on. The final hour is devoted to a description of the important agencies, private, semiprivate and public, that are devoted to child welfare.

The instruction that the students now receive in the outpatient department is more important. Stanford has recently adopted a plan of medical instruction under which all seniors spend the entire morning in the clinics, observing and, under supervision, actually doing much of the work. In the study of pediatrics, they have six mornings a week for four weeks in the clinics. The Children's Clinic, with us, has become a community health center. At least 60 per cent of our patients are well infants and children, and a considerable proportion of the remainder come because of minor complaints in order that they may not become major complaints. We have the large group of healthy infants brought to us primarily for direction in feeding; they are given regular physical examinations and on suspicion have blood counts, Wassermann tests, urinalyses, etc., made. Visits to the homes by the nurses are reported here and the condition in the homes correlated with the medical diagnosis. The discovery and control of contact with tuberculosis and other communicable diseases are important phases of the work both with infants and with older children. We make systematic efforts to have every child given the specific preventive treatments—especially vaccination and toxin-antitoxin—and every student gives these to at least one patient, and per-

forms the Schick and Dick tests. He becomes familiar with the detection and treatment of congenital syphilis through the careful scrutiny and testing given every prospective mother and her infant after birth, and with the energetic early antisyphilitic treatment.

The student sees also something of what can be accomplished by persistent and long continued direction and control of a large group of children—half orphans, orphans, and children of tuberculous parents—placed in foster homes by our Associated Charities, whose medical direction is entrusted to us.

He is familiarized with the control of acute contagious disease, with the problem of the mental defective and with the care of the child having heart disease. He learns to look for early decay of the teeth and to instruct mothers and children in the importance of the tooth brush. He looks for flatfeet, postural defects and other orthopedic deformities in order that they may be detected and corrected during the plastic age.

Special attention is given to disease conditions of the eye, ear, nose, mouth and throat, and to the essential preventive value of such examinations in childhood.

So striking is the preponderance of preventive work in the children's clinic that the student, seeing all of it and actually doing a large part of the work himself, cannot fail to become imbued with the idea that his function in practice in later years will be not only to care for the sick, but also to do all he can to promote the health of his patients, particularly his juvenile patients.

Dr. L. T. Royster, University of Virginia: Until and through the year 1923, there was no pediatric department in the School of Medicine at the University of Virginia. In that year a new wing of the hospital had just been completed and was dedicated to obstetrics and children's diseases, and the newly born infants were turned over to the pediatric department at birth. Within a reasonable time, a small building was erected adjacent to the outpatient department, and in this was housed the pediatric outpatient activities. The accommodation for children in the hospital at the present is approximately seventy beds, including those for newly born infants, medical pediatrics, orthopedic and surgical cases and certain cases of eye, ear, nose and throat diseases.

In the development of this department, three outstanding advantages appeared to me: First, no traditions of administration were established necessitating revolutionary changes; second, since no money was appropriated, a free hand was allowed the head of the department in dispensing any money that was donated from private sources for the conduct of the department; third, the University of Virginia is situated in the mountains of Virginia, in close proximity to a people, a large proportion of whom are relatively uninfluenced by modern civilization, whose available food is unbalanced, and whose children have never been under observation from a pediatric standpoint.

For clinical and teaching purposes, the pediatric department is divided into two main branches: (1) the hospital service—almost entirely remedial in its efforts except for newly born infants, care of these being largely in the prevention of disease; (2) the outpatient department, subdivided into (*a*) a daily clinic for sick and well children (as far as possible, seen on different days) and (*b*) field work in the mountains of Virginia. This is given in addition to classroom lectures.

In the hospital, fourth year students work in sections for six weeks at a time on each major service. Comparison between the normal and abnormal child cannot well be made in the wards but, even here, an effort is made to point out to the student how far each child differs from the normal, and how this particular

illness could have been prevented. In the nursery—the service for the newly born—care of the normal infant is stressed and preventive pediatrics is taught intensively.

In the outpatient department, third year students are assigned to this service for two months, and daily clinics of two and a half hours are held. In the well child division of the clinic, the evidence of what may be called a normal child is emphasized and deviation from the normal demonstrated. In the presence of the students, the instructors give talks in the care and feeding of children and sanitary home conditions, special stress being placed on how to keep a well child well.

All children, either sick or well, who attend the clinic are followed up in their homes by a trained public health nurse, accompanied by a student nurse from the hospital. The students themselves are also required to visit some of the homes of the children seen by them in the clinic and to submit a written survey of the conditions observed, with their recommendations for improvement of the conditions found. All of this work is credited on the class standing.

One or two field clinics in the mountain districts are held every week, in the public schools, mission schools, churches or private residences. These clinics are attended by the head of the department or his assistant, accompanied by one of the hospital interns, a group of students, the field nurse assigned to that particular district and one or more student nurses from the training school. After these clinics are held and recommendations made, the children are followed up in their homes by the field nurse. Children who require attention at the clinic or in the hospital for remedial purposes are brought in by the nurses, sometimes a distance of forty or fifty miles.

In the field work, a beginning is made for prenatal instruction.

We realize that the larger proportion of children are still attended by the family physician, and it is beginning to be recognized that the objects of public health can best be attained through the practice of prophylactic pediatrics. We have therefore acted on the assumption that the majority of every graduating class will enter general practice and that in teaching pediatrics the pediatric needs of the general practitioner should be stressed.

In the outpatient department, the student gains his impression of what he is to face in private practice and is trained in the methods to follow when he meets the problems of nutrition, and all of the phases of the application of preventive medicine through the administration of prophylactic inoculation and instruction in the personal hygiene of the children.

Dr. John A. Foote, Georgetown University, Washington, D. C.: In its department of medicine, which is about 76 years old, such an institution as Georgetown University has no state aid or no heavy private endowment, either.

The third year students take up pediatrics, and the work is divided into two semesters. There are 160 hours of instruction in pediatrics in the third year. The first eighty hours are devoted practically entirely to the consideration of the normal child. In other words, in those eighty hours the students are taught normal physiology and elementary nutrition.

Because of the important part that the diseases of the new-born and deaths of the new-born play in the scheme of mortality, the students are given instruction didactically and clinically in the care of the new-born and diseases of the new-born. A number of men are grouped around this division. Some prepared meritorious, rather elementary papers on the care of the new-born and diseases of the new-born, which I gathered together and which we use as a textbook; thus thirty hours are devoted to the diseases of the new-born.

Up to two years ago, we were fortunate in our clinical facilities. At that time there was at our university hospital a flourishing child hygiene center, where students were taught in groups. The Health Department took over the child health department, which broke up our personnel. Then the hospital started an extensive building program, which curtailed the room, so that for the last two years we have been obliged to abandon the teaching clinic in the child hygiene department of the university hospital. However, we now have a fine Child Hygiene Center in the Children's Hospital, where most of our other clinical work is being done; two assistants of our division of pediatrics are in that center, and we have made arrangements with them in our new curriculum to have students work there. The center is open every day; we have an average of fifty patients a day, and we conduct nutrition classes—infant and preschool divisions of the clinic. Our men will work in that department next year. Meanwhile, groups of students are taken throughout the year in the wards of the hospital, and during the first part of the session we try to emphasize the normal child, normal configuration and normal characteristics. We try to get as nearly normal children as we can, and to teach these men how to handle the child. We try to make these young men familiar with the normal characteristics of the child, and to obtain some practical knowledge of the nutritional requirements of the child.

Later in the year, we have some of the groups visit a milk plant and study the methods of safe milk marketing. They are taught about milk and its modifications in the outpatient department, and in a general way we try to give them practical knowledge in the elementary health needs of the normal child. That is particularly stressed in the second half of the session. We think it is important because if these men are to go out in practice, they must not suffer from pediphobia —that is, they must not be afraid of the child. Dr. Wall last year spoke of the fact that the average medical student was rather afraid of the very young infant. Now, if we give students sufficient experience in handling children, in actually putting their hands on them, that fear will not be present.

DISCUSSION

DR. CLIFFORD G. GRULEE: I do not intend to tell my own experiences in teaching, but I want to give you some of the national background which makes it exceedingly difficult for the pediatric department to function in the way that it should.

I recently made a survey of seventeen of the leading schools in the country as to the proportionate amount of required work in pediatrics in the last two years, and I find that on the average the proportionate amount required in pediatrics is one seventeenth of the schedule in the last two years, but, unfortunately, I have to confess that my school is below that average. The highest amount that was given in pediatrics in the last two years was one seventh.

This should be kept in mind when I tell another thing, and that is that the National Board of Medical Examiners do not recognize pediatrics as a separate subject, and when the secretary of that board was quizzed on that subject, his letter said that he occasionally put in a question in pediatrics in the branch of internal medicine. When general medicine is as far behind as that, the men who are carrying the load of pediatrics in the country are going to have a hard time to put over the work that they think should be put over and feel must be put over, in regard to the teaching of child health and preventive work among children, in the medical schools.

As I conceive of a department of pediatrics, there are four separate subheads under which we must teach. We must teach, above all things, diseases of the new-born, because among the new-born children there has been no reduction in mortality rate, or practically none, in the last twenty years. Second, we have the branch which we are discussing here, that is, preventive work. Third, we have contagious diseases, which is rather a large field but is probably the smallest of the four.

Then we have that field of diseases of infancy and childhood which properly covers the same field as internal medicine does today in any of our medical schools.

When one has such a vast problem as that to contemplate, one must see that we are limited in the amount of work we can give in preventive medicine in the courses which we can give to an already overloaded medical student. He has already too much work to do, and to force an excessive amount of work on his shoulders is unfair. The question is what to do, and I confess I do not know. I think that the two things we must force in order to get the proper recognition are first, to see that the general medical world recognizes the necessity for more pediatrics in the medical school and second, see that the students give proper recognition to this, because it is the only department, as departments in the medical schools now are run, which prepares a man for general practice. The departments of internal medicine and surgery are breaking up into specialties already. I do not know how it is in other medical schools, but in the one in which I teach, practically all the teaching, especially in the department of internal medicine, is done by specialists in diseases of the chest, the heart, gastro-intestinal diseases, diabetes and nephritis; and each one feels that he must have his clinic. The only one who covers the whole realm of medicine is the pediatrician.

I think there is no question but that the men who are teaching pediatrics recognize the value of teaching the promotion of child health and preventive medicine, but we have certainly a hard problem before us in order to put this thing over as it should be.

---

## CHICAGO PEDIATRIC SOCIETY

*Regular Meeting, March 15, 1927*

GEORGE E. BAXTER, M.D., *President, in the Chair*

A NEW MICRO-PRECIPITATION TEST FOR SYPHILIS. INAUGURAL THESIS. DR. M. G. PETERMAN.

This paper will be published in full.

DISEASES OF THE SKIN AS SEEN IN AN OUTPATIENT CLINIC FOR CHILDREN. DR. EDWARD A. OLIVER (by invitation).

In his experience at the Children's Memorial Hospital, Dr. Oliver has found that eczema requires the supervision of both the pediatrician and the dermatologist. All the children treated there were thoroughly examined, and a diet was outlined by the pediatrician before dermatologic treatment was instituted. In the majority of cases, excellent results were obtained with crude coal tar ointment, as advocated by White, and a 10 per cent naphthalan ointment combined with 2 per cent sulphonated bitumen, N. N. R. Most of the patients went on to complete clinical recovery, though some required observation for two or three years.

Dr. Oliver discussed the hemangiomas and classified them as (1) those of the flat nevus flammeus type; (2) the capillary nevi of the strawberry type and (3) the deeper, cavernous type. In the last two types, excellent results were obtained with radium, while carbon dioxide snow was of value in lesions of the strawberry type. In treating the deeper, cavernous type of lesion, the radium was usually screened with 3.3 mm. rubber, and the time allowed for exposure varied from one hour at the first treatment to one and three-fourths hours. With the strawberry type of lesion, the screening was 0.2 mm. aluminum and a thin piece of rubber. Carbon dioxide snow was used for those cases in which the cosmetic result was not to be carefully considered.

Pityriasis rosea in children was discussed, for while not nearly as common as in adult life it is frequently seen in the children's clinic. The youngest patient that Dr. Oliver had seen with this disorder was a child, aged 3.

Eczematoid ringworm, so common in adults, was uncommon in this clinic. Psoriasis also was rarely seen.

Erythema multiforme and erythema nodosum were occasionally seen, but in none of the cases of the latter disorder was any evidence of tuberculosis found. Tuberculosis of the skin was only occasionally encountered.

Two cases of lichen scrofulosorum and two of scrofuloderma had been treated in the past six years.

Ringworm of the scalp constituted one of the common disorders, but only infrequently had it been necessary to resort to epilation with the roentgen-ray to effect a cure. Various antiseptic ointments—iodine crystals in goose grease, white precipitate ointment, Whitfield's ointment of salicylic and benzoic acid and chrysarobin—were the drugs used.

Skin diseases in children differ relatively little from those seen in adults, and, aside from the group of eczemas respond more readily to treatment than they do in adults.

DISCUSSION

Dr. S. C. Henn: Is it possible to have pityriasis rosea in a child, aged 1 year? I saw one with a herald spot ten days before the eruption.

Dr. Oliver: I do not recall any report of a case in a child that young.

Dr. Jesse R. Gerstley: Is there any explanation for the action of tar in these eczematous cases? I have heard it said that any effect obtained is due to the phenol and not to the tar itself.

It may interest Dr. Oliver to know that some cases of poisoning are reported in young infants from the use of sulphur in scabies.

Dr. George E. Baxter: Have you had any experience with the use of the ultraviolet ray in the treatment of eczema?

Dr. Albert H. Roler: I did not understand about the treatment of lichen urticatus and should like to hear more about it.

Dr. Arthur H. Parmelee: The question of erythema nodosum has interested me. I have seen four cases in the last two years, two of which I feel sure were tuberculous in origin. One case occurred in a physician's child who was about 4 years of age and who had definitely been exposed to tuberculosis. After the erythema nodosum disappeared, roentgen-ray examination of the chest showed the primary focus and involvement of the bronchial glands. The child has been followed for a period of eight months by roentgen-ray examinations, and everything points to a definite tuberculosis. In one instance there was some doubt as to whether the case was tuberculous or not. One case

occurred following an indurative pneumonia of long duration. The onset occurred in January, and the case was followed until August by roentgen-ray and physical examinations, without any change being evident, until in August, an erythema nodosum developed and roentgenogram taken three weeks later and physical examination showed almost complete resolution of the process. Whether the acute rise in temperature and the development of erythema nodosum had anything to do with the resolution of the indurative process I cannot say. One sees a great deal in the literature, especially the German, about the connection between erythema nodosum and tuberculosis, but I am sure that other toxins may have something to do with the development of the disorder.

DR. CLIFFORD G. GRULEE: The last case referred to by Dr. Parmelee follows closely the cases described abroad, as epituberculous infiltration. It seems to me that one would have to follow the case for a much longer period than the few months that have elapsed in order to say that the condition was not tuberculous.

DR. PARMELEE: This case has been followed constantly, and negative reactions were obtained in four Pirquet tests. The lung is absolutely clear except for a line of thickened pleura, and there is nothing in the child's condition at present that points toward tuberculosis.

DR. OLIVER (closing): I have been asked to repeat the prescription I mentioned. It consists of crude coal tar, 2 parts; Burrow's solution, 5 parts; wool fat, 10 parts, and enough zinc paste to make 30 parts.

Answering Dr. Gerstley, I think the soothing effect of the tar is due to its phenol content. The crude coal tar itself, while possibly irritating, has a beneficial effect on the inflamed skin. It is necessary to have a coal tar that is thoroughly washed; otherwise, irritation and frequent pus infections result from its use.

The ultraviolet ray has been used in many cases of eczema, and I believe its good effects in children are due to its building up the general bodily resistance.

In answer to Dr. Parmelee, I have been on the lookout for tuberculosis in cases of erythema nodosum but have not encountered any showing evidence of the disease. Stokes reported one case in this country, and the patient developed generalized tuberculosis with a fatal termination. Several years ago, Dr. Parmelee mentioned the coincidence of tuberculosis and erythema nodosum, and I have been watching for it ever since.

---

## ST. LOUIS PEDIATRIC SOCIETY

*Regular Meeting, May 6, 1927*

THE WORK OF THE CHILDREN'S CENTER (A BEHAVIOR CLINIC). DOROTHY CROUNSE.

For years, not only physicians and social workers but lay people as well have realized that there is a reason for all types of behavior and that when this behavior has been undesirable in any way, there has been a tendency to assign it to some physical defect. With the development of the mental hygiene movement, has come the realization that undesirable traits and habits of personality are not necessary evils.

The Children's Center was first established in 1925 in the congested lower southeast central side of St. Louis. In November, 1926, the center moved to its present location at McPherson and Euclid. The staff of the center consists of two full time social workers, one of whom also acts as director of the center, a part time psychologist, a part time psychiatrist, a part time pediatrician, and a full time secretary.

Children up to 12 years of age are accepted for study and treatment, but the preschool and early school age are preferred. Seemingly well adjusted children are occasionally accepted for study, particularly the children of organizations that place children where it is desirable to know each child and his particular needs thoroughly. The only children under 12 years not accepted for study at the center are those having outstanding cases of mental defect or advanced mental disorder, in whom treatment in the clinic would not be of avail. We are particularly interested in children who are showing signs of maladjustment through the development (1) of unwholesome personality traits such as sensitiveness, seclusiveness, day dreaming, fanciful lying, laziness, selfishness, timidity and cowardliness, unpopularity, hyperactivity and the like; (2) undesirable habits such as thumb sucking, nail biting, enuresis, masturbation, mannerisms, peculiar food fads, sleep disturbances, etc., and (3) children who are showing signs of maladjustment as indicated by undesirable behavior such as disobedience, teasing, bullying, temper tantrums, bragging, defiance of or rebellion against authority, lying, stealing, truancy, cruelty, sex activities, destructiveness and the like.

Examination is made from four angles: A psychologic examination on all children of school age is made to show, approximately, with what we are dealing from the standpoint of intelligence; a social history is obtained in order that we may know what the heredity and environment of the child are; a physical examination is made to rule out physical causes for the particular maladjustment; and a psychiatric examination is made to learn what the mental content of the child's mind is, what are his interests, attitudes, hopes, conflicts, fears, etc. No medical treatment is given at the Children's Center, and when the need is found, the child is referred to his own physician and a report of our examination given him. When there are no physical symptoms, treatment is carried on in the center by the psychiatrist, and necessary adjustment in the community are engineered by the social worker.

We have our successes and our failures, and from every child we learn something new concerning both the study and the treatment of problems in behavior. Such a clinic is in reality a research laboratory, but one in which definite formulas and processes can never be determined because we are working with personalities and no two problems are ever the same. Of one thing we are sure, namely, that the happy and well adjusted child is the healthy child, and real health is not found when there is maladjustment and its concomitant, unhappiness.

STUDIES ON SCARLET FEVER. DR. JEAN V. COOKE.

In a study of the skin sensitivity to scarlatinal streptococcus filtrate toxin on 200 new-born infants and their mothers, it was found that in the first two weeks of life the infants' skin did not react to small amounts of scarlatinal toxin and that it reacted to large amounts in only a small proportion of cases. In some who gave negative reactions, antitoxin was demonstrable in the blood, but those without demonstrable antitoxin also gave negative reactions in a large proportion of cases. When tested two months later, only about 5 per cent of the infants reacted to small doses of toxin in the skin, although about 25 per cent more gave reactions

to large amounts. In tests on groups of older infants and children of varying ages it was found that the skin reaction to a small amount of toxin, which was noted in only a small proportion in the first six months, increased rapidly in the last half of the first year, and was highest (more than 60 per cent, during the second year. After the sixth year there was a definite decrease in the proportion of children whose skin reacted to the toxin. The presence of antitoxin in the blood was more or less constantly demonstrable in older children whose skin reactions were negative to small doses of toxin.

MINOR ENDOCRINE DISTURBANCES OF CHILDHOOD. DR. LOUIS COHEN.

In his paper, Dr. Cohen described:

1. The common misapprehension concerning endocrinology—especially in reference to the frequency, manifestations, physiologic and pathologic characteristics, and treatment of endocrine diseases and an undue enthusiasm of its disciples.

2. A discussion of some of the basic principles of endocrinology.

3. The etiology and pathogenesis of endocrine disturbances, with particular reference to the subject of heredity.

4. A discussion of the symptoms and signs of infantile and juvenile hypothyroidism, and its relation to mental retardation and juvenile delinquency.

5. A discussion of symptoms and signs of juvenile hypopituitarism—anterior lobe, posterior lobe, and bilobar cases—and their relation to genital maldevelopment and the secondary psychic aspects.

6. A discussion of minor aberrations of the pineal, suprarenal and sex glands.

7. Illustrative cases, histories and slides.

# Book Reviews

KAUSALE FERMENT-THERAPIE DER INFEKTIONSKRANKHEITEN. F. SCHÜRER-WALDHEIM. Neue Heilkunde und Gesundheitslehre, Heft V. Oldenburg: R. Schwartz, 1927. Pp. 20. Price, Rm. 2.

The author proposes a new procedure for immunization. It is based on the experimental work of Abderhalden, who found that antitoxins produced in the animal organism have the nature and characteristics of ferments; hence the name "Abwehrfermente," which was coined by him. He developed the theory that the animal organism utilized ferments in this manner as a defense mechanism.

On the basis of Abderhalden's theories, the author conceived the idea of introducing parenterally foreign proteins combined with the toxin of the disease in question, in the hope that this combined stimulus would produce the antibody ferment. These ferments, in turn, would break down the toxic protein substances and in this manner neutralize the harmful effect of pathogenic organisms.

Horse serum and ox serum were used as foreign protein, and the urine of the patient affected with the specific infectious disease was used as the vehicle containing the toxin of such a disease.

From 0.5 to 2 cc. of serum combined with an equal amount of urine in dilution of 1:16 drops to 100 cc. distilled water, or a weaker solution — 1 drop to 300 to 400 cc. of distilled water — were used. The injections were given every three to seven days.

The optimal combination for adults seemed to be 5 cc. of serum to 0.5 cc. of urine, with a smaller dosage for infants. The author reports marvelous results, particularly in chronic types of infection such as chronic and subacute polyarthritis, progressive paralysis, chronic sepsis and other conditions. In estimating the author's claims, it is difficult to escape the impression that they are rather fantastic and exaggerated and not based on sound reasoning or well authenticated experimental fact. It is hardly conceivable that physicians will readily accept this procedure for immunization without far more substantial clinical proof than the author presents in this publication.

THE DISEASES OF INFANTS AND CHILDREN. By J. P. CROZER GRIFFITH, AND A. GRAEME MITCHELL. Second Edition, volumes 1 and 2. Vol. 1, 461 illustrations; 20 plates in color; pp. 788. Vol. 2, 461 illustrations; 20 plates in color; pp. 927. Price, $20.00. Philadelphia: W. B. Saunders & Co., 1927.

This work, of two volumes, is perhaps the most complete book on pediatrics written by any two men. Not only are the authors' own views expressed, but also there are given in the text references to all the important works on the various subjects under discussion. It is hard to overvalue a work of this kind, since it has in it so much that is of use, and since it has not neglected that personal element which is so valuable in any textbook. One cannot pick out a chapter here and there as most deserving of praise, because the book throughout is of the same general character. The general practitioner or the pediatrician will find in it a comprehensive résumé on almost any subject

in pediatrics. The illustrations are excellent and well chosen, and the numerous color plates are especially good.

"The Diseases of Infants and Children may be used as a reference book because of its numerous quotations and references. Taken all in all, it is the most comprehensive pediatric textbook that is now to be found in any language, as far as the reviewer knows. If there is any criticism to be offered it is in the fact that the portion of the book devoted to infant feeding is far too complicated for the average physician. The attempt here has been not to advocate any one way of feeding but to present all views. To the reviewer's mind, this is a mistake. In all, the book is worthy of praise, and this second edition will be found as useful as the first, with additions in the text showing the advance of knowledge in pediatrics during the interval.

DIE VITAMINE. By RAGNAR BERG. Second Edition. Pp. 714. Leipsic: S. Hirzel, 1927.

After an interval of about three years, Berg has found it necessary to issue a second edition of his work on the vitamins. He states that during this time over 5,000 larger and smaller articles have appeared on the nutritional factors and closely related fields. There is no work on this subject which contains such a wealth of literature and bibliographic references. There are in all almost 100 pages devoted to a consideration of the literature, comprising some 3,450 references, an increase of 1,900 over the first edition.

The title of this work is somewhat misleading, as a large part of it is devoted to subjects other than the vitamins. For example, there are chapters on the biologic value of the proteins, on the importance of the mineral constituents and on conditions affecting growth. One of the most interesting chapters is that which considers mineral metabolism. As is well known, Berg has always stressed the great importance of a diet containing an excess of bases and the harmfulness of one in which acids preponderate.

The book is characterized by an individual point of view and is by no means a mere statement of current opinion. This fact makes it all the more interesting, although from time to time one may differ with the author. It is a work which can be highly commended and should be invaluable to those who are actively interested in the field of nutritional disorders, a field which is encumbered by a literature so voluminous that it has become increasingly difficult to cope with it.

CLINICAL PHYSIOLOGY. By ROBERT J. S. MCDOWALL, with an introduction by W. D. HALLIBURTON. Price, $7.00. Pp. 363. New York: D. Appleton & Co., 1927.

The author presents an altogether timely treatise which takes up physiology from an entirely different standpoint. The book is well written and readable. The English is excellent, and the incidents chosen are apt. The first part of the book is taken up largely with the part of physiology that deals with the nerves, including the special senses. The cardiovascular system is next taken up, together with the blood and then the lungs. The structure of the gastro-intestinal, as well as the genito-urinary, system is given several pages. The remaining chapters deal with body neutrality, water content of the body, temperature of the body, exercise and rest, protection against disease, the skin, the autonomic nervous system, the balance of endocrine organs and the treatment of emergencies, with an appendix on metabolism. The book is not only

useful from a practical standpoint, but the reading of it often suggests, here and there, problems for investigation. This is not to be regarded as an exhaustive treatise; rather, it is an attempt to interest the physician and student in clinical physiology.

THE ARTIFICIAL LIGHT TREATMENT OF CHILDREN IN RICKETS, ANAEMIA AND MALNUTRITION. By KATHERINE M. L. GANGEE, with introduction by PROF. LEONARD HILL. Price, $4.00. Pp. 168. New York: Paul B. Hoeber, Inc., 1927.

The reviewer knows of no other book that treats so thoroughly the practical and theoretical aspects of artificial light therapy. The range of wave lengths furnished by the various types of lamps and the proper care and testing of the apparatus, as well as the question of dosage, are considered. The author shows the need of artificial light in the big industrial areas and discusses in detail the management and equipment of the light clinics. Case reports are given, and there are many excellent illustrations and plates. The appendix gives the Royal Society chart of electromagnetic waves, and a discussion of Vitaglass, which allows the passage of ultraviolet rays, and of the cadmium photo-electric cell for the detection of ultraviolet waves.

# Directory of Pediatric Societies

## NATIONAL

### AMERICAN MEDICAL ASSOCIATION, SECTION OF DISEASES OF CHILDREN

Chairman: Dr. Hugh McCulloch, 500 S. Kingshighway, St. Louis.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Minneapolis. Time: To be decided later.

### AMERICAN PEDIATRIC SOCIETY

President: Dr. J. Claxton Gittings, 1828 Pine St., Philadelphia.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Washington, D. C. Time: April 30 to May 2, 1928.

### THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Place: Minneapolis. Time: Spring.

### AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Undecided. Time: May or June, 1928.

### CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto, Canada.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto, Canada.
Place: Vancouver, B. C. Time: June, 1928.

## SECTIONAL

### CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. O. L. Goehle, 15703 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. H. T. Price, 121 University Place, Pittsburgh.
Place: Cleveland. Time: Oct. 14 and 15, 1927.

### SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

President: Dr. Robert A. Strong, Pass Christian, Miss.
Secretary: Dr. Hugh L. Dwyer, Medical Arts Bldg., Kansas City, Mo.
Place: Memphis, Tenn. Time: Nov. 14 to 17, 1927.

**LOCAL**

### PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

### BROOKLYN PEDIATRIC SOCIETY

President: Dr Harold L. Barnes, 1235 Dean St., Brooklyn.
Secretary: Dr. Charles A. Weymuller, 61 Greene Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

### BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St., and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

### CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.
Secretary: Dr. Frank J. Williams, 58 South Swan St., Albany, N. Y.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

### CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

### THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. Henry J. Gerstenberger, 2103 Adelbert Road, Cleveland.
Secretary: Dr. Charles W. Burhans, 2103 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

### DETROIT PEDIATRIC SOCIETY

President: Dr. Thomas B. Cooley, 987 Jefferson Avenue, East, Detroit.
Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

## LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.

## MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 So. Bellevue Ave., Memphis, Tenn.
Secretary: Dr. Arthur G. Quinlan, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

## MILWAUKEE PEDIATRIC SOCIETY

President: Dr. Roy M. Greenthal, 141 East Wisconsin Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

## NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

## PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. William Ropes May, 8 East 66th St., New York.
Secretary: Dr. Stafford McLean, 17 East 71st St., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

## NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. C. F. Gelston, 384 Post St., San Francisco.
Secretary: Dr. Mary H. Layman, 2116 Pacific Ave., San Francisco.
Place: Alternates between Stanford University Hospital, University of California Hospital, and Children's Hospital. Time: Three or four times a season.

## NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schlutz, Univ. of Minnesota, Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

## PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

## THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.

Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.

Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

## ST. LOUIS PEDIATRIC SOCIETY

President: Dr. T. Wistor White, Lister Bldg., St. Louis.

Secretary: Dr. E. H. Rohlfing, 816 Beaumont Medical Bldg., St. Louis.

Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

## SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.

Secretary: Dr. Wm. Sidney Bowers, 1136 W. 6th St., Los Angeles.

Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

## TEXAS PEDIATRIC SOCIETY

President: Dr. Lucius Hill, San Antonio.

Secretary and Treasurer: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.

Place: Houston. Time: December, 1927.

## PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. W., Toronto.

Secretary: Dr. F. R. Hassard, 1361 King St. W., Toronto.

Time: November 17, December 15, February 16 and March 15.

THE AMERICAN JOURNAL OF DISEASES OF CHILDREN is published by the American Medical Association as a means for the advancement of knowledge of the diseases of children and for the publication of scientific investigation in this field.

Manuscripts for publication, books for review, and correspondence relating to the editorial management should be sent to Dr. Clifford G. Grulee, 310 South Michigan Avenue, Chicago, or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, AMERICAN JOURNAL OF DISEASES OF CHILDREN, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the AMERICAN JOURNAL OF DISEASES OF CHILDREN. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the AMERICAN JOURNAL OF DISEASES OF CHILDREN is covered by copyright; but, as a rule, no objection will be made to its reproduction in reputable medical journals, if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the AMERICAN JOURNAL OF DISEASES OF CHILDREN or in any one of the other publications issued by the American Medical Association will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The AMERICAN JOURNAL OF DISEASES OF CHILDREN is published monthly. Annual subscription price (two volumes): Domestic, $4.00; Canadian, $4.30; foreign, $4.50, including postage. Single copies, 50 cents, postpaid.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

## OTHER PERIODICAL PUBLICATIONS
### of the American Medical Association

**THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION**—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $6.50; foreign, $7.50. Single copies, 20 cents.

**ARCHIVES OF INTERNAL MEDICINE**—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 75 cents.

**ARCHIVES OF NEUROLOGY AND PSYCHIATRY**—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

**ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY**—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

**ARCHIVES OF SURGERY**—Monthly. Devoted largely to the investigative and clinical phases of surgery, with monthly reviews on orthopedic and urologic surgery. Well illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

**ARCHIVES OF OTOLARYNGOLOGY**—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

**ARCHIVES OF PATHOLOGY AND LABORATORY MEDICINE**—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

**QUARTERLY CUMULATIVE INDEX MEDICUS**—Quarterly. A complete subject and author index to the worth-while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $8.00; Canadian, $8.50; foreign, $8.75.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. CHICAGO

# CONTENTS


PAGE

Mikulicz's Syndrome: A Report of Ten Cases. Alexander J. Schaffer, M.D., and A. Wilmot Jacobsen, M.D., Baltimore ..... 327

Anemia in Children, with Splenomegaly and Peculiar Changes in the Bones: Report of Cases. Thomas B. Cooley, M.D.; E. R. Witwer, M.D., and Pearl Lee, M.D., Detroit ..... 347

Antirachitic Properties of Irradiated Dry Milk. G. C. Supplee, Ph.D., and Odessa D. Dow, M.S., Bainbridge, N. Y. ..... 364

Cirrhosis of the Pancreas and Liver in an Infant. Cornelia De Lange, M.D., Amsterdam, The Netherlands ..... 372

Talipomanus: A Report of Three Cases in One Family. Edgar E. Martmer, M.D., Detroit ..... 384

Rickets: An Unusual Roentgenographic Manifestation. Philip Lewin, M.D., Chicago ..... 388

The Heart and Blood Vessels in Congenital Syphilis. Irving Matusoff, M.D., and Paul D. White, M.D., Boston ..... 390

Microprecipitation Test for Syphilis. M. G. Peterman, M.D., Milwaukee ..... 404

Prevention and Treatment of Thrush (Oidial Stomatitis). Harold K. Faber, M.D., and Esther B. Clark, M.D., San Francisco ..... 408

Etiology of Respiratory Disease in the City and Country School of New York City. Edith M. Lincoln, M.D., New York ..... 418

Chvostek's Facialis Sign in New-Born Infants. Frank E. Stevenson, M.D.; A. Graeme Mitchell, M.D., and Carl A. Koch, M.A., Cincinnati ..... 425

Gastric Digestion: The Relation of the Hydrogen Ion Concentration Volume and Buffer Capacity of the Gastric Contents to a Milk Test Meal. Raymond B. Miles, M.D., Brooklyn, and Alfred T. Shohl, M.D., New Haven, Conn ..... 429

Mushroom Poisoning Due to Hebeloma Crustuliniforme: Report of Four Cases. H. W. Price, M.D., Baltimore ... 441

Progress in Pediatrics:

Evidence of Rickets Prior to 1650. John A. Foote, M.D., Washington, D. C. ..... 443

News and Comment ..... 453

Abstracts from Current Literature ..... 456

Society Transactions:

American Child Health Association ..... 501

Book Reviews ..... 518

Directory of Pediatric Societies ..... 521